A DISSERTATION ON
"A STUDY ON CLINICAL AND BIOCHEMICAL CORRELATION BETWEEN VARIOUS TYPES OF SEIZURES AND PSEUDOSEIZURES"

Submitted to

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For the Award of the Degree of

M.D. BRANCH –I: GENERAL MEDICINE

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CERTIFICATE BY THE INSTITUTION

This is to certify that **Dr.SRIDHAR.S.P,** Post - Graduate Student (ACADEMIC YEAR 2016 - 2019) in the Department of General Medicine, Government Stanley Medical College, Chennai- 600 001, has done this dissertation on **"A Study on Clinical and Biochemical Correlation between Various Types of Seizures and Pseudoseizures"** under my guidance and supervision in partial fulfillment of the regulations laid down by The Tamil Nadu Dr. M.G.R. Medical University, Chennai, for M.D. (General Medicine), Degree Examination to be held in May 2019.

Dr.R.MUTHUSELVAN, M.D.,
Professor and HOD
Department of General Medicine,
Govt. Stanley Medical College & Hospital,
Chennai – 600001.

Dr.S. PONNAMBALA NAMASIVAYAM, MD, DA, DNB.,
Dean
Govt. Stanley Medical College &Hospital,
Chennai –600001.

CERTIFICATE BY THE GUIDE

This is to certify that **Dr.SRIDHAR.S.P,** Post-Graduate **(ACADEMIC YEAR 2016 - 2019)** in the Department of General Medicine, Government Stanley Medical College, Chennai- 600 001, has done this dissertation on **"A Study on Clinical and Biochemical Correlation between Various Types of Seizures and Pseudoseizures"** under my guidance and supervision in partial fulfilment of the regulations laid down by The TamilNadu Dr.M.G.R.Medical University, Chennai, for M.D. (General Medicine), Degree Examination to be held in April 2019.

Dr.R.MUTHUSELVAN, M.D.,
Professor and Head of Department,
Department of General Medicine,
Govt.Stanley Medical College and Hospital,
Chennai – 600001.

DECLARATION

I, **Dr.SRIDHAR.S.P,** declare that I carried out this work on **"A Study on Clinical and Biochemical Correlation between Various Types of Seizures and Pseudoseizures"** at the Department of General Medicine, Government Stanley Medical College and Hospital. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, or diploma to any other university board either in India or abroad.

This is submitted to **The Tamil Nadu Dr.M.G.R.Medical University, Chennai** in partial fulfillment of the rules and regulation for the M. D. Degree examination in General Medicine.

Dr.SRIDHAR.S.P

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Dr.SRIDHAR.S.P

CERTIFICATE

This is to certify that this dissertation work titled **"A Study on Clinical and Biochemical Correlation between Various Types of Seizures and Pseudoseizures",** done by the candidate Dr.SRIDHAR.S.P with Registration Number-201611062 for the award of M.D. in the branch of GENERAL MEDICINE. I personally verified the http://www.urkund.com/en/website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows SEVEN percentage of plagiarism in the dissertation.

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CONTENTS

INTRODUCTION

Differential diagnosis between epileptic seizures, especially between complex partial seizures (CPS) and pseudo seizures is a common diagnostic problem. The variety of ways in which seizures and pseudo seizures are expressed has made their diagnosis difficult, particularly because the patient frequently cannot describe either the nature or the duration of events. Investigations such as electroencephalogram (EEG) may aid diagnosis but are never diagnostic in isolation. Reliance solely on EEG patterns can sometimes lead to both false positive, and false negative diagnoses.

Thus, the diagnosis of epilepsy on the basis of typical signs, symptoms, or routine laboratory tests is not an easy task. Diagnosis is further complicated by the close resemblance of some types of seizures to a variety of other neurological, psychiatric, and medical disorders.

Prolactin (PRL) release from the pituitary is controlled by the hypothalamus via a PRL inhibitory factor, now believed to be dopamine. It has been hypothesized that ictal epileptic activity in the mesial temporal structures may propagate to the hypothalamus, altering the hypothalamic regulation of PRL release. Prolactin elevation has been described following generalized tonic–clonic and complex partial Seizures. Consequently, the determination of prolactin serum levels

(SPRL), immediately after the attack, has been used as an ancillary investigation in differentiating between seizures and pseudo-seizures. To test this hypothesis, we examined the dynamics of serum prolactin concentrations after the epileptic attack and after pseudo-seizures.

REVIEW OF LITERATURE

SEIZURE

Seizure is defined as paroxysmal event that occurs due to abnormal excessive or synchronous neuronal activity. Depending on the distribution of discharges, abnormal brain activity can present as various manifestation ranging from dramatic convulsive activity to experiential phenomena that may not be readily discernible by an observer.

Although the incidence and prevalence of seizures are influenced by various factors approximately 5–10% of the population will have an episode of at least one seizure, in their lifetime. With incidence of occurrence of seizure highest in early childhood and late adulthood.

EPILEPSY

Epilepsy is defined as two or more unprovoked seizures. Hence epilepsy is a condition in which a person has recurrent seizures, which may be due to a chronic underlying process. Therefore, a person with a single episode seizure, or recurrent seizures due to correctable causes, does not necessarily have epilepsy. Since, there are many causes and types of Epilepsy, it is not a single disease entity, in fact it refers to a clinical phenomenon. Based on specific underline aetiology, clinical and pathologic characteristic, there are various epilepsy syndromes which are described below.

The incidence of epilepsy is ~0.3–0.5% in different populations throughout the world, and the prevalence of epilepsy is 5–10 persons per 1000.

CLASSIFICATION OF EPILEPSY

The International League against Epilepsy (ILAE) Classification and terminology.

1. Focal Seizures

Can be further described as having motor, sensory, autonomic, cognitive, or other features.

2.Generalised Seizures

- Absence seizures
  - Typical
  - Atypical
- TONIC CLONIC
- CLONIC
- TONIC
- ATONIC
- MYOCLONIC

3.May be focal, generalised, or unclear

Epileptic spasms

Determining type of seizure is important for focusing on further diagnostic approach and for selecting appropriate therapy because different drugs acts by different mechanism and also effective against

particular types of seizures and also for determining further prognosis. This classification is based on the clinical features of seizures and associated findings on electroencephalograph. This classification does not take into consideration distinctive features such as cellular substrate or aetiology. This classification system which is based on clinical feature and electroencephalographic findings may change in future as advanced imaging technology and cellular biology helps us to learn more and more about s mechanisms that underlie different seizure types.

Seizures may be either focal or generalised. Nowadays term partial seizures not used. Focal seizures originate from single cerebral hemisphere or networks that are limited to single cerebral hemisphere. Focal seizures are usually due to structural abnormalities in brain. Generalized seizures usually arise from multiple cerebral hemispheres or networks that are distributed across multiple cerebral hemispheres. In contrast, generalized seizures may occur due to structural abnormalities, biochemical, or cellular disturbances. However, there may be some exception in both types of seizure. Other features are described below.

FOCAL SEIZURES

Focal seizures originate from single cerebral hemisphere or networks that are limited to single cerebral hemisphere. Focal seizures are usually due to structural abnormalities in brain. Older classification of simple focal seizure and complex focal seizures are not used

nowadays. Newer classification is based on presence or absence of cognitive impairment.

SUBCATIGORIES OF FOCAL SEIZURE

- ❖ Focal seizure with dyscognitive features
- ❖ Focal seizure without dyscognitive features

Focal seizures can also progress to generalized seizures. In older system it was termed as focal seizures with secondary generalization.in newer system it was described as focal seizure with secondary generalisation and also type of generalised seizure that evolve from focal seizure.

As with other types of seizures investigation of diagnosis is electroencephalogram.

Electroencephalogram may show brief epileptiform discharge or spikes or sharp waves. Sometimes interictal electroencephalogram may be normal. This is because most of focal seizures arise from medial temporal lobe or inferior temporal lobe. These regions are distant from the scalp, the electroencephalogram recorded may be nonlocalizing these patients, seizure focus can be identified by using sphenoidal or surgically placed intracranial electrodes.

Focal Seizures without Dyscognitive Features

Focal seizures can occur without impairment of cognition. Focal seizures can also cause motor symptoms, sensory symptoms, autonomic symptoms or psychic symptoms.

Focal Motor Seizure

Seizure occurring from right primary motor cortex near area controlling foot movement may present as involuntary movements of contralateral foot which may either be clonic and pure tonic posturing at a frequency of ~2–3 Hz; seizures arising from motor cortex that controls hand may be associated with involuntary movements of contralateral and abnormal movements of face because motor cortex for facial expression is in the area adjacent to the cortical region that is controlling hand movement. The electroencephalogram recorded during seizures may show epileptiform spikes in region over appropriate area of cortex. Seizures arising from deeper brain structures may not be recorded by scalp electrodes. In such patients sphenoid or surgically placed electrodes may be helpful.

Jacksonian March and Todd's Paralysis

In some patient's involuntary movements may occur in very restricted area which may progress to larger portion of extremity over seconds to minutes. This phenomenon is explained by Hughlings

Jackson hence it is also named as jacksonian march. And this denotes spread of seizure activity to larger portion of motor cortex.

Some patients also experience localised paresis known as Todd's paralysis, which may last for minutes to hours following seizures.

EPILEPSIA PARTIALIS CONTINUA

It is a type of focal motor seizure in which seizure may continue for hours to days. Epilepsia partialis continua is difficult to treat as it is refractory to most of the antiepileptic drugs.

Focal sensory seizures

Features of focal sensory seizures include somatic sensation such as parathesia, visual symptoms such as flashing lights or formed hallucinations, sensation of falling or vertigo.

Focal seizures with autonomic features

Focal seizures can present with autonomic features such as flushing, piloerection, sweating.

Focal seizures with other features

Focal seizures can present as sensation of intense odours or unusual smell, or sounds, or epigastric sensation that arises from stomach or chest to head. Some patients may present with symptoms of aura such as fear, depersonalisation, dejavu and illusions.

FOCAL SEIZURES WITH DYSCOGNITIVE FEATURES

Focal seizures can also present with transient impairment in consciousness. Seizure usually begins with aura. The start of ictal phase is marked by sudden motionless stare or behavioural arrest. The behavioural arrest is followed by automatisms such as chewing, swallowing, lip-smacking, picking movements of hands. Sometimes patients may present with behaviours such as running and emotional behaviour. These patients do not respond to any visual command or verbal command during an episode of seizure and they also have poor recollection of events that occurred during ictal phase. The patient is usually confused after seizure episode recovery of consciousness may occur within seconds or it may take up to hours. On clinical examination of after the seizure episode patient may have antegrade amnesia or postictal aphasia if seizure focus occurs in dominant hemisphere. Since behaviours linked to focal seizure is very broad one should be very cautious before labelling patient has atypical behaviour or psychiatric problems. In these scenario's detailed electroencephalogram studies can be helpful.

SECONDARY GENERALISATION OF FOCAL SEIZURE

IF focal seizure spread to both cerebral hemisphere it may produce generalised seizure of clonic, tonic, or clonic -tonic types. But usually it may present as generalised seizure with clonic-tonic type. Secondary generalisation of focal seizure usually occurs in seizures

arising from frontal lobe but it may occur in focal seizures occurring anywhere in brain. Secondary generalisation of focal seizure is often difficult to distinguish from primary onset generalised seizure. This is because accompanying attenders usually emphasize more on generalised convulsive phase of seizure and they often miss out focal symptoms which present at onset of seizure. Hence careful history may helpful in picking up focal symptoms and preceding aura. Differentiating these two types is important because diagnostic approach and treatment modality is different for these two types of seizures. Careful history and thorough electroencephalogram studies are usually helpful.

GENERALISED SEIZURES

Generalised seizure usually occurs with involvement of both cerebral lobes. It is proposed that seizure focus arise at some point in the brain but it may rapidly spread to neuronal network in both cerebral hemispheres. Different types of generalised seizures and their features or discussed below.

TYPES OF GENERALISED SEIZURES

1. Absence Seizures
2. Clonic
3. Tonic
4. Clonic-Tonic
5. Myoclonic

ABSENCE SEIZURES

There are Two Types of Absence Seizures

- Typical
- Atypical

TYPICAL ABSENCE SEIZURES

It is most common seizure in 15-20% of children with epilepsy. Typical Seizures are characterised by sudden brief onset of loss of consciousness lasting only for seconds. There will be no loss of postural control. Consciousness returns immediately. There will be no post ictal confusion. Absence seizures are also accompanied by subtle, bilateral motor signs such as chewing, clonic movements of hands and rapid blinking of eyes. Sometimes loss of consciousness is the only manifestation of seizures and there may be no motor signs. Hyperventilation usually provokes seizures. In typical absence seizure, usual onset of age is 4-8 or early adolescence. One typical feature of absence seizure is that it may occurs hundred times per day but children may unaware or unable to tell their existence. Since clinical features are subtle, most of the children present with history of day dreaming and poor school performance.

DIAGNOSIS

Investigation of choice is electroencephalogram.

Electroencephalogram usually shows generalised, symmetric,3-Hz spike and wave discharge that starts and ends suddenly, superimposed on a normal electroencephalogram. Periods of spike-and-wave discharges occur for more than a few seconds and it also correlates with clinical signs. The electroencephalogram also shows many more brief bursts of abnormal cortical activity. Hyperventilation will provoke seizures and electrographic discharges. Hence it is routinely used at the time of electroencephalogram studies.

ATYPICAL ABSENCE SEIZURES

Atypical absence seizures as name suggests have features that are different both clinically and electro physiologically from typical absence seizures. Children may present with less abrupt onset, and longer duration of seizure episode. Seizure may also be accompanied by more motor signs.

Atypical absence seizures occur due to diffuse or Multifocal structural abnormalities of the brain. Hence it is also associated with other signs of neurologic dysfunction frequently mental

Retardation. Furthermore, the atypical absence seizures are poorly responsive to anticonvulsants when compared to typical absence seizures which make it difficult to treat.

DIAGNOSIS

Diagnosis of atypical absence seizure can be made using electroencephalogram. Electroencephalogram shows a generalized, slow spike-and-wave pattern and

Frequency is usually of ≤2.5 per second.EEG may also show abnormal activity that may not correlate with clinical signs.

GENERALIZED, TONIC-CLONIC SEIZURES

Generalized-onset tonic-clonic seizures is the most common seizure when compared to other types of seizures.it represents almost 10% of all persons with epilepsy. It is also the most common Seizure type that occurs due to metabolic derangements. Hence it more commonly encountered in many different clinical scenarios. The onset of seizure is usually abrupt and there may not be any warning signs. Sometimes patient may describe some discomfort before the onset of seizure. This prodrome is different from the stereotypic auras that are usually seen with focal seizures that generalize. During initial phase of the seizure usually, there will be tonic contraction of muscles that occur throughout the body. Patient may show different clinical features depending on the muscle groups involved.

A loud moan or ictal cry that occur at the onset of seizure is due to tonic contraction muscles of expiration and muscles of larynx. Due to tonic contraction of muscles of expiration respiration is impaired, there

is pool of secretion in the oropharynx and cyanosis results due to impaired respiration and oxygenation of blood.

Contraction of the jaw muscles causes biting of the tongue. Heart rate and blood pressure increases and pupils dilate due to increased sympathetic tone. Tonic phase of seizure is usually followed by clonic phase after 10-20 seconds which is characterised by periods of muscles relaxation which is superimposed on tonic muscle contraction.

Clonic phase which is marked period of muscles relaxation increases until end of seizure. Clonic phase usually lasts for less than one minute. The postictal phase is characterized by altered consciousness, unresponsiveness, decreased muscle tone, and excessive salivation that may sometime causes stridor during breathing and partial airway obstruction. Bladder or bowel incontinence may occur in post ictal period. Patients regain consciousness gradually over minutes to hours, and during this period of transition, patient may have typically a period of postictal confusion. After recovery from post ictal period Patients may subsequently complain of headache, muscle ache, and fatigue which may last many hours. Duration of Postictal phase may vary depending on duration of seizures and other accompanying central nervous system disease and other systemic disease. Postictal phase is usually long in patients with prolonged seizures and in patients with

other underlying disease Such as cerebral atrophy due chronic alcoholism.

Variants of generalised tonic-clonic seizures:

1) Pure tonic seizures
2) Pure clonic seizures

There are number of other variants of GTCS of which pure tonic seizures lasting for only a few seconds is important because they are usually associated with epileptic syndromes such as lennox-Gastaut syndrome which will be discussed below.

DIAGNOSIS

The EEG recorded during the tonic phase of the seizure will show a progressive Increase in generalized low-voltage fast activity, which will be followed by Generalized high-amplitude, polyspike discharges.

The EEG recorded during clonic phase will show the high-amplitude activity is interrupted by slow waves to create a spike-and-wave pattern. The postictal EEG will show diffuse slowing that will recover gradually as the patient awakens.

ATONIC SEIZURES

Atonic seizures are usually characterized by sudden loss of postural muscle tone which will be lasting for 1–2 seconds. Consciousness will be impaired.

But there is will be no associated postictal confusion. Features of atonic seizures include quick dropping of head or nodding movement if seizure is very brief to collapse of the patient if seizure occurs for a longer duration. Seizure occurring for longer duration is associated with increased risk for patient because loss tone may cause direct head injury due to fall.as with pure tonic seizures atonic seizures are also commonly associated with epilepsy syndromes.

DIAGNOSIS

The EEG will show brief, generalized spike-and-wave discharges which will be followed immediately by diffuse slow waves that occurs due to loss of muscle tone.

MYOCLONIC SEIZURES

Myoclonus is characterised by sudden and brief muscle contraction that may involve entire body or any one part of the body. A most common normal physiologic form of myoclonus is the sudden jerking movement that occurs while falling asleep. Pathologic myoclonus is most commonly associated with metabolic disorders, degenerative CNS diseases, or anoxic brain injury.

Myoclonic seizures are caused by cortical, subcortical or spinal dysfunction. Hence it should be considered as a true epileptic event. Myoclonic seizures and other forms of generalized seizures are usually

coexisting. Myoclonic seizure is the predominant feature of juvenile myoclonic epilepsy.

DIAGNOSIS

EEG will show bilaterally synchronous spike-and-wave discharges. These spike and wave discharges are synchronous with the myoclonus but synchronisation can be obscured by artefact due to muscle contraction.

UNCLASSIFIABLE SEIZURES

Not all seizure fit into focal or generalized, and therefore they should be labelled as unclassifiable, until there is sufficient evidence to allow a valid classification.

Epileptic spasm is one of unclassifiable seizures which are characterised by sustained brief flexion or extension of proximal muscles including truncal muscles Epileptic spasms occur due to difference in nerve functions and connections in immature versus mature CNS hence it is most commonly seen in infants.

DIAGNOSIS

The EEG in these patients will show hypsarrhythmias.

Hyparrhythmias are nothing but diffuse, giant slow waves with a background of multifocal spikes and sharp waves which are usually irregular. During an episode of The clinical spasm, there will be marked

suppression of the EEG background which is known as “electro decremental response”.

The electromyogram (EMG) are helpful in differentiating spasms from brief tonic and Myoclonic seizures with epileptic spasms. In epileptic spasms EMG will show a characteristic rhomboid pattern.

EPILEPSY SYNDROMES

Epilepsy syndromes are disorders in which epilepsy is a predominant feature, and through clinical, EEG, radiologic, or genetic observations suggest a common underlying mechanism. Three common epilepsy syndromes are discussed here

1) Juvenile myoclonic epilepsy

2) Lennox-gastaut syndrome

3) Mesial temporal lobe epilepsy syndrome

JUVENILE MYOCLONIC EPILEPSY

Juvenile myoclonic epilepsy (JME) is a generalized seizure disorder, cause for seizure is not known. Family history suggests that cause may be polygenic.it usually occurs in early adolescence. JME is characterized by bilateral myoclonic jerks which may be single or repetitive. The myoclonic seizures occur most frequently in the morning after awakening from sleep. It can be provoked by sleep deprivation. There will be no loss of consciousness during seizures but it can be lost

in severe myoclonic seizures' one third of the patient may have absence seizures. Some patients also experience generalized tonic-clonic seizures. Seizures in JME usually responds well with treatment but complete remission is rare.

LENNOX-GASTAUT SYNDROME

Lennox-Gastaut syndrome occurs most commonly in children .it is triad of

1) multiple seizure including GTCS, atonic and atypical absence seizures

2) EEG showing slow<3hz spike and wave discharge impaired cognitive function

CAUSES:

CNS Dysfunction due to

- Perinatal hypoxia
- Developmental abnormalities
- Trauma/ infection

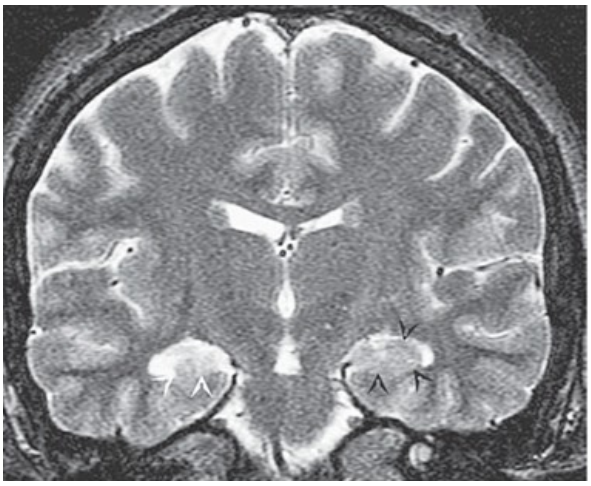
Many patients have a poor prognosis, which is mainly due to poor control of epilepsy and underlining CNS disease.

MESIAL TEMPORAL LOBE EPILEPSY SYNDROME

Mesial temporal lobe epilepsy (MTLE) is the most common syndrome associated with focal seizures with dyscognitive features. It is refractory to antileptics. But responds well to surgical treatment.

DIAGNOSIS

High-resolution MRI shows characteristic hippocampal sclerosis.



Coronal high resolution T2 weighted image shows abnormal high-signal intensity in right hippocampus consistent with mesial temporal lobe sclerosis White arrow – normal black arrow –abnormal

CHARACTERISTIC OF MESIAL TEMPORAL LOBE SCLEROSIS

History

- ❖ History of febrile seizures
- ❖ Family history of epilepsy
- ❖ Early onset
- ❖ Rare generalized seizures

- Seizures may remit and reappear
- Seizures often intractable

Clinical Observations

- Aura common post ictal disorientation
- Behavioural arrest/stare memory loss
- Complex automatisms dysphasia
- Unilateral posturing

Laboratory Studies

- Unilateral or bilateral anterior temporal spikes on EEG
- Hypometabolism on interictal PET
- Hypoperfusion on interictal SPECT
- Material-specific memory deficits on intracranial amobarbital (Wada) test

MRI Findings

- Small hippocampus with increased signal on T2-weighted sequences
- Small temporal lobe
- Enlarged temporal horn

- ❖ Pathologic Findings
- ❖ Highly selective loss of specific cell populations within hippocampus

Genes associated with epilepsy syndromes:

GENE	SYNDROME
CHRNA4(20q13.2)	Autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE)
KCNQ2(20q13.3)	Benign familial neonatal convulsion(BFNC)
SCN1B(19q12.1)	Generalised epilepsy with febrile seizures plus(GEFS+)
LGI1(10q24)	Autosomal dominant partial epilepsy with auditory features(ADPEAF)
EPM2A(6q24)	Progressive myoclonus epilepsy (Lafora's disease)
Doublecortin(Xq21-24)	Classical lissencephaly associated with severe mental retardation and seizures
CSTB(21q22.3)	Progressive myoclonus epilepsy (unverricht-lundborg disease)

THE CAUSES OF SEIZURES AND EPILEPSY

Neonates (<1 month)	Perinatal hypoxia and ischemia
	Intracranial hemorrhage and trauma
	Acute CNS infection
	Metabolic disturbances (hypoglycemia, hypocalcemia, hypomagnesemia, pyridoxine deficiency)
	Drug withdrawal
	Developmental disorders
	Genetic disorders
Infants and children (>1 month and <12 years)	Febrile seizures
	Genetic disorders (metabolic, degenerative, primary epilepsy syndromes)
	CNS infection
	Developmental disorders
	Trauma
	Idiopathic
Adolescents (12–18 years)	Trauma
	Genetic disorders
	Infection
	Brain tumor
	Illicit drug use
	Idiopathic
Young adults (18–35 years)	Trauma
	Alcohol withdrawal
	Illicit drug use
	Brain tumor
	Idiopathic
Older adults (>35 years)	Cerebrovascular disease
	Brain tumor
	Alcohol withdrawal
	Metabolic disorders (uremia, hepatic failure, electrolyte abnormalities, hypoglycemia, hyperglycemia)
	Alzheimer's disease and other degenerative CNS diseases
	Idiopathic

DRUGS CAUSING SEIZURES

Alkylating agents (e.g., busulfan, chlorambucil)

Antimalarials (chloroquine, mefloquine)

Antimicrobials/antivirals

β-lactam and related compounds

Quinolones

Acyclovir

Isoniazid

Ganciclovir

Anesthetics and analgesics

Meperidine

Tramadol

Local anesthetics

Dietary supplements

Ephedra (ma huang)

Gingko

Immunomodulatory drugs

Cyclosporine

OKT3 (monoclonal antibodies to T cells)

Tacrolimus

Interferons

Psychotropics

Antidepressants

Antipsychotics

Lithium

Radiographic contrast agents

Theophylline

Sedative-hypnotic drug withdrawal

Alcohol

Barbiturates (short-acting)

Benzodiazepines (short-acting)

Drugs of abuse

Amphetamine

Cocaine

Phencyclidine

Methylphenidate

Flumazenil[a]

DIFFERENTIAL DIAGNOSIS FOR SEIZURES

Syncope

- ❖ Vasovagal syncope
- ❖ Cardiac arrhythmia
- ❖ Valvular heart disease
- ❖ Cardiac failure
- ❖ Orthostatic hypotension

Psychological disorders

- ❖ Psychogenic seizure
- ❖ Hyperventilation
- ❖ Panic attack

Metabolic disturbances

- ❖ Alcoholic blackouts
- ❖ Delirium tremens
- ❖ Hypoglycemia
- ❖ Hypoxia

Psychoactive drugs

- ❖ (E.g., hallucinogens)

Migraine Transient ischemic attack (TIA)

- ❖ Basilar artery TIA

Sleep disorders

- ❖ Narcolepsy/cataplexy
- ❖ Benign sleep myoclonus

Movement disorders

- ❖ Tics
- ❖ Nonepileptic myoclonus
- ❖ Paroxysmal choreoathetosis

Special considerations in children

- ❖ Breath-holding spells
- ❖ Migraine with recurrent abdominal
- ❖ pain and cyclic vomiting
- ❖ Benign paroxysmal vertigo
- ❖ Apnoea
- ❖ Night terrors
- ❖ Sleepwalking
- ❖ Basilar migraine
- ❖ Confusional migraine

DIAGNOSTIC WORK UP FOR SEIZURE

1) Electrophysiologic Studies

2) Magnetoencephalogram(MEG)

3) Brain imaging – CT brain, MRI brain volumetric studies

4) Baseline investigations – Complete blood count

- Renal function test/liver function test

- Serum electrolytes

ELECTROPHYSIOLOGIC STUDIES

All patients who Presented with seizure disorder, EEG should be Done as soon as possible.

In patients who presented with suspected epilepsy, EEG should be done and presence of abnormal discharge having discrete onset and termination clearly concludes diagnosis. However, the absence of electrographic seizure activity does not exclude a diagnosis of a seizure disorder, this is because focal seizures that originate from inferior temporal lobe and medial temporal lobe are difficult to pick up with scalp electrodes.

In patients with general tonic-clonic seizure EEG are not always abnormal. Since seizures are always infrequent and unpredictable, it is not possible to record the EEG during the seizure episode. In these scenario's continuous monitoring using video-EEG telemetry units for longer periods in hospitalized patients. For ambulatory patients, portable equipment can be used to record the EEG continuously on cassettes for ≥24 hours. Video-EEG telemetry is now a used as routine investigation

for the accurate diagnosis of seizures in patients with poorly characterized events or seizures.

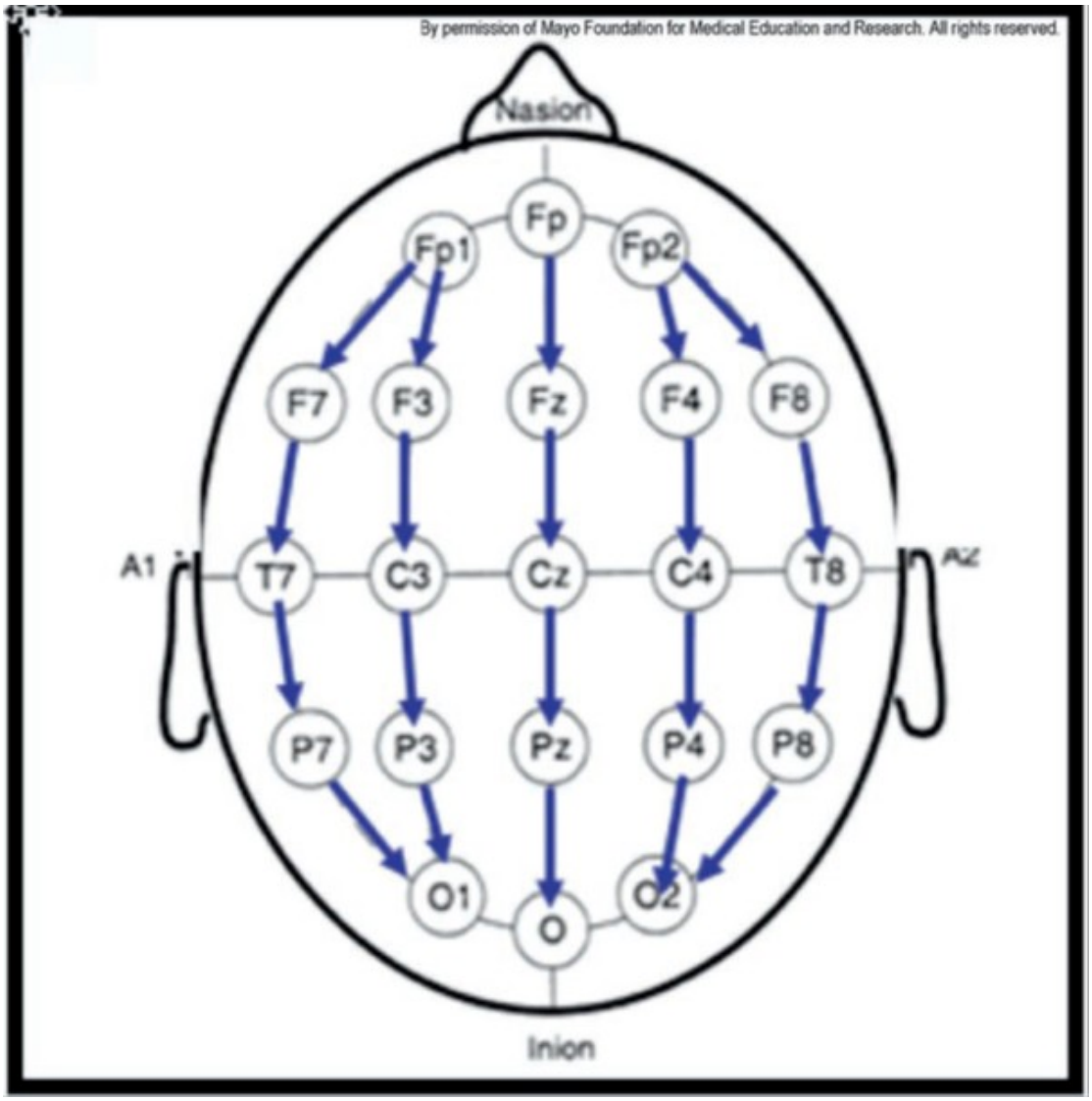
The EEG can also be used for diagnosis of seizure during interictal period which may show certain abnormalities such as burst of abnormal discharges containing spikes or sharp waves that are highly indicative of the diagnosis of seizure disorder.

The presence of epileptiform activity is not specific for diagnosis of epilepsy, but such epileptiform activity is highly prevalent in patients with epilepsy than normal person. EEG cannot establish the diagnosis of epilepsy because routine interictal EEG can be normal up to 60% of time. The EEG is also helpful in classifying seizure disorders and aiding in the selection of anticonvulsant medications.

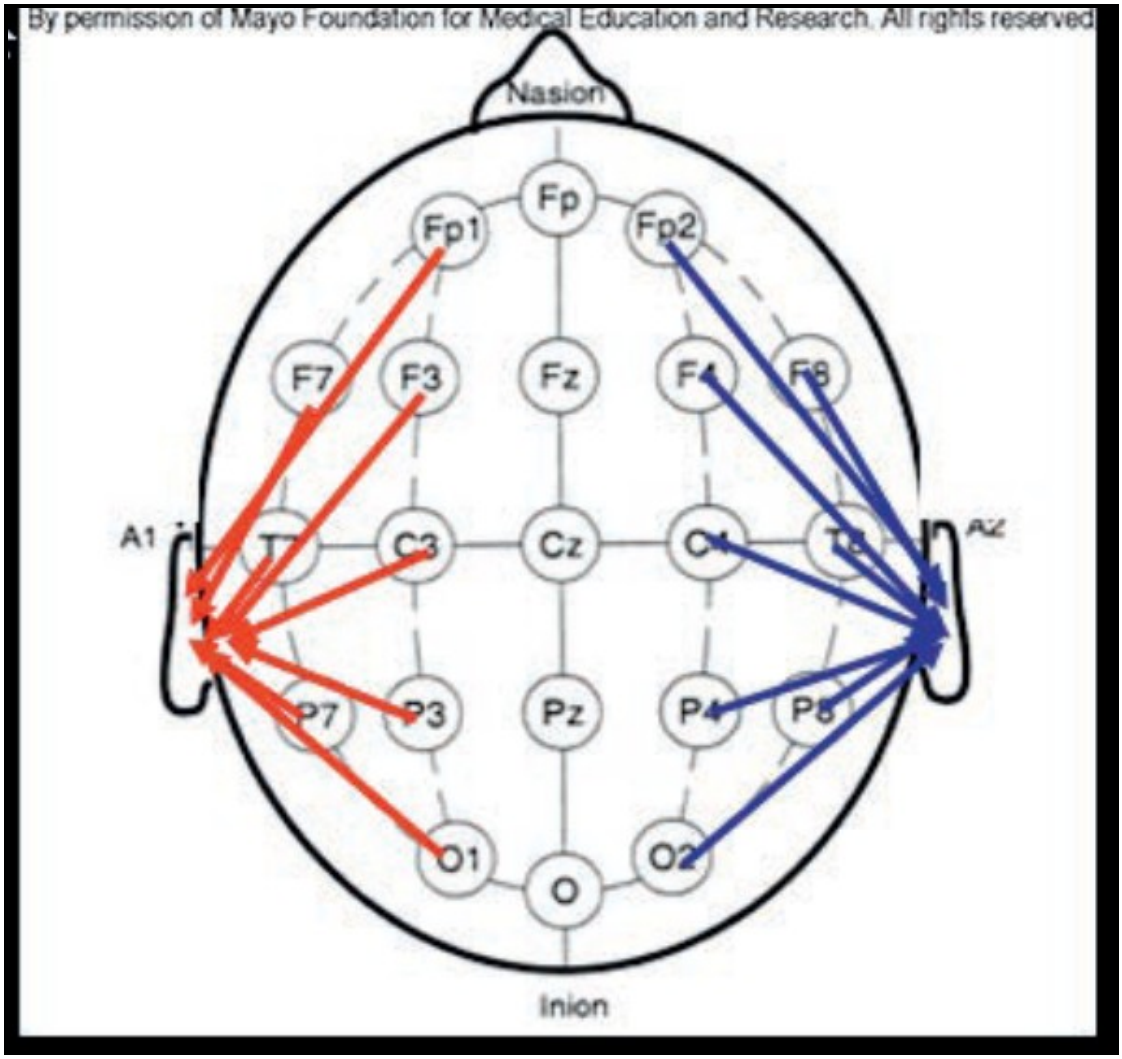
The routine scalp-recorded EEG may also helpful in assessing the prognosis of seizure disorders; In general, patients with a normal EEG has better prognosis than patients with abnormal background or profuse epileptiform activity. Unfortunately, the EEG has not proved to be helpful in predicting whether patients with predisposing conditions such as head injury or brain tumour, will develop epilepsy in future.

Normal EEG with typical montage. An example of the EEG recorded during wakefulness in a 24-year-old woman. This is a 10-second duration epoch. The first four channels, together referred to as a chain, show cerebral activity recorded from the midline head region and by convention are arranged front to back. The next four channels, the second chain, show activity over the left parasagittal head region. The middle four channels, the third chain, shows the corresponding right parasagittal region. The two bottom sets of four channels, or chains, each show the left and right temporal head regions, respectively. Each division shows 1 second of recording time. There is faster sinusoidal rhythmic activity that is most prominent in each set of four channels over the occipital regions or posterior channels and is approximately symmetric. This is the PDR, best seen when the eyes are closed during relaxed wakefulness. The broadly contoured, downward deflection in the 2nd second in each of the five frontal channels represents an eye-blink artefact, as does the similar wave in the 9th second. An ECG channel is

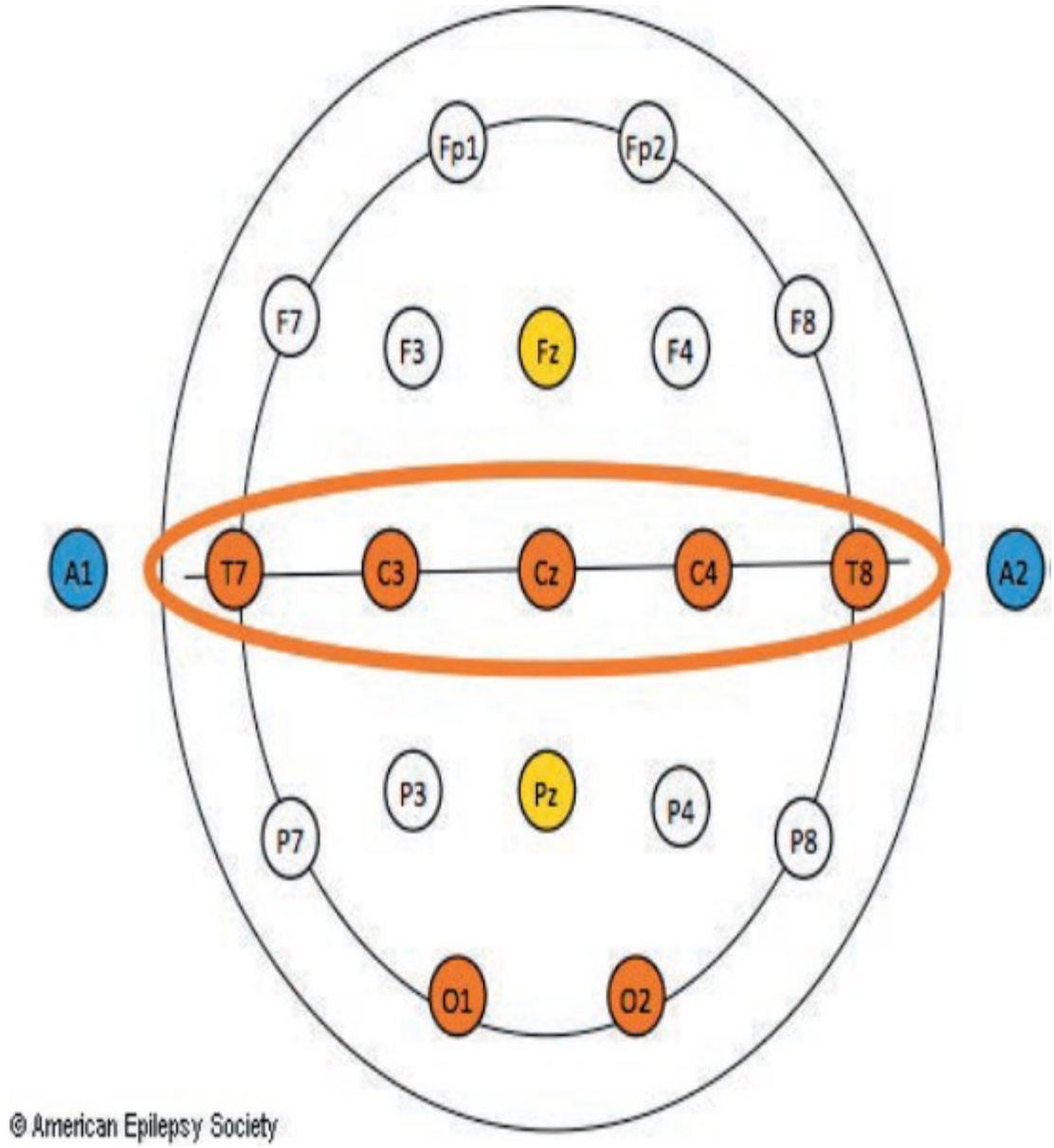
displayed at the very bottom, which helps the interpreter to detect the cardiac cycle (a common source of artefacts contaminating the EEG channels) and possible cardiac dysrhythmias.



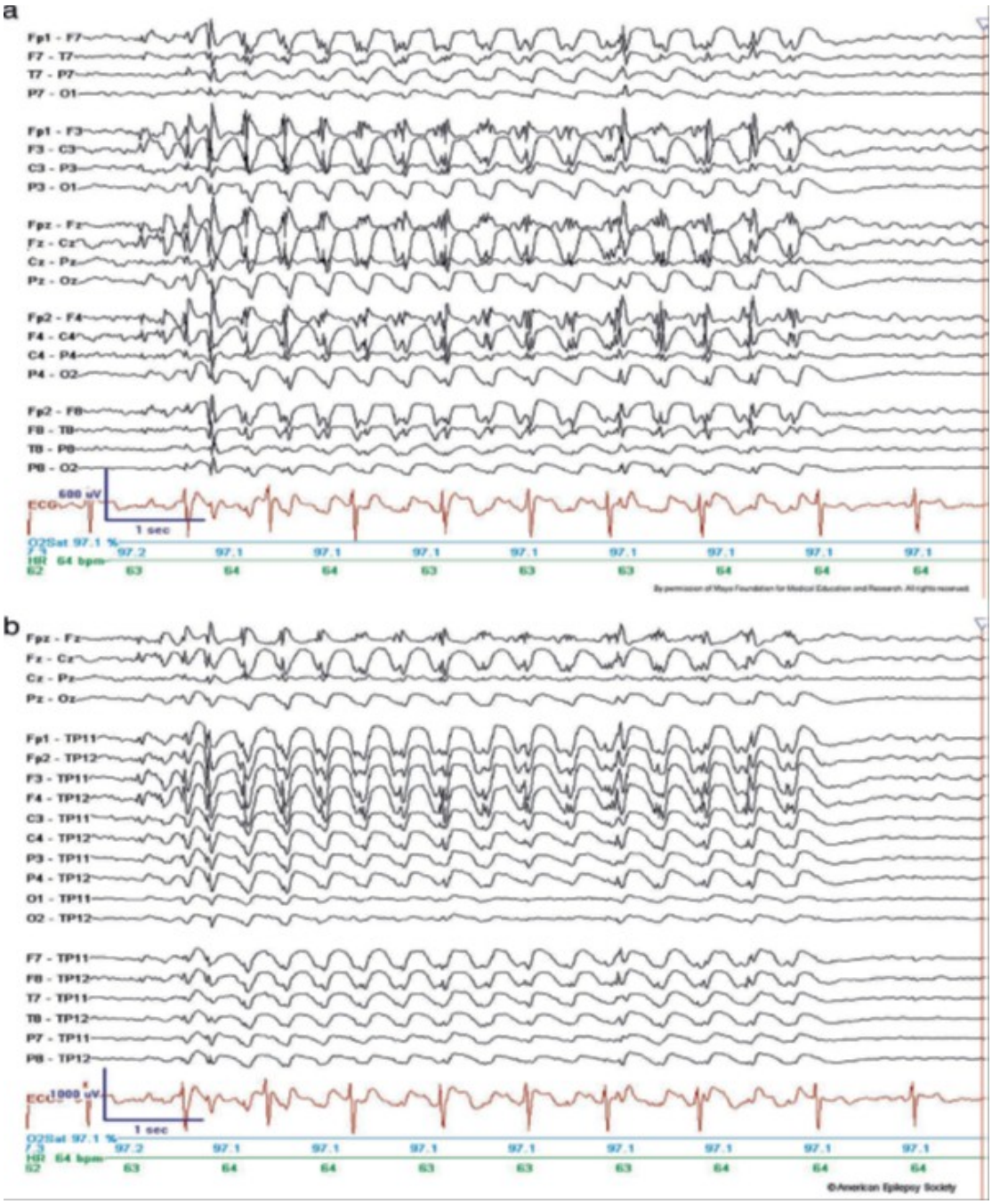
The International 10-20 electrode placements. Showing a longitudinal bipolar montage. Copyright 2013. Mayo Foundation for Medical Education and Research. All rights reserved. Courtesy of Dr. Jeffrey W. Britton, MD.



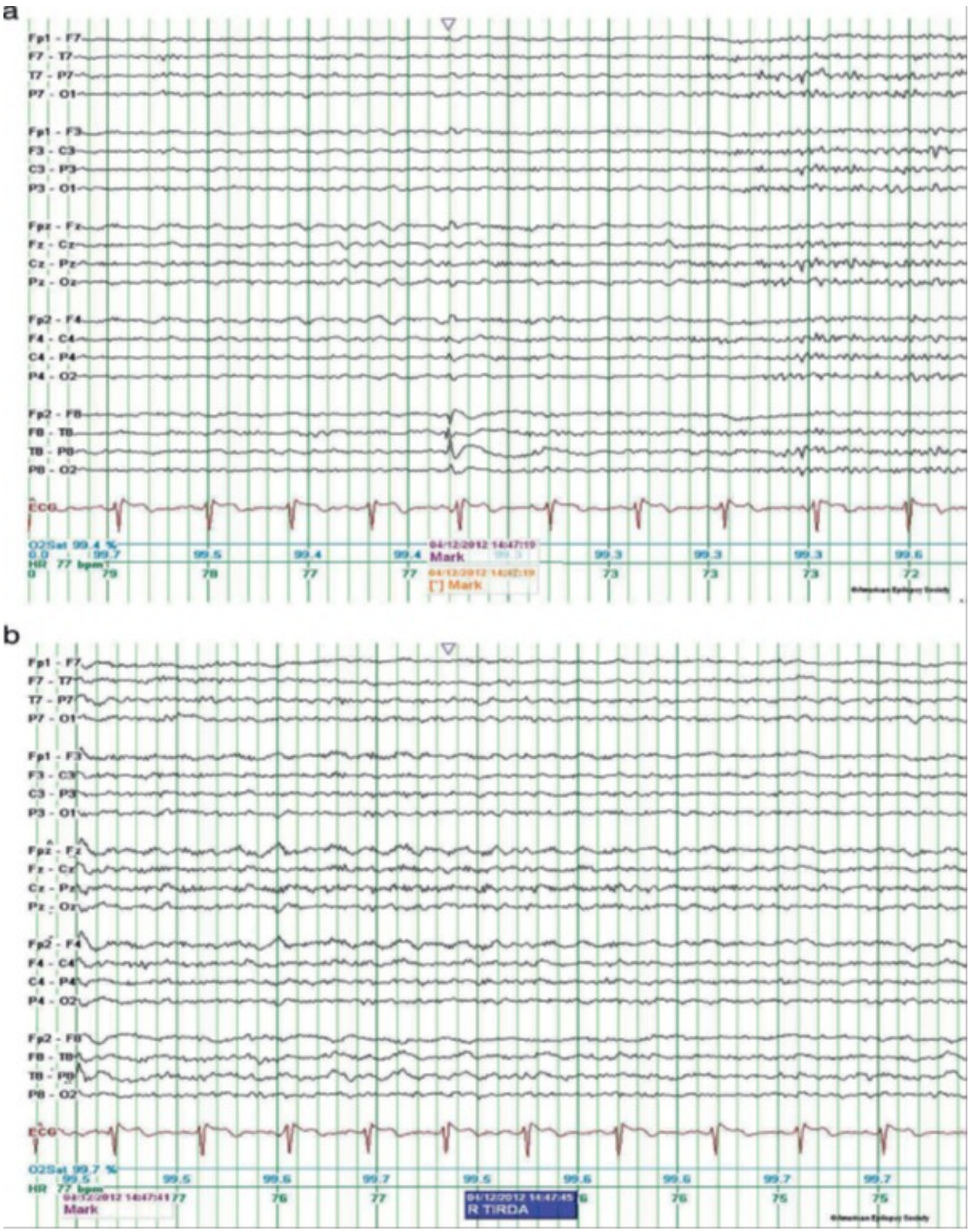
Ipsilateral ear referential montage. EEG electrode placement using the International 10-20 electrode placement system. Copyright 2013. Mayo Foundation for Medical Education and Research. All rights reserved. Figure courtesy of Jeffrey W. Britton, MD.



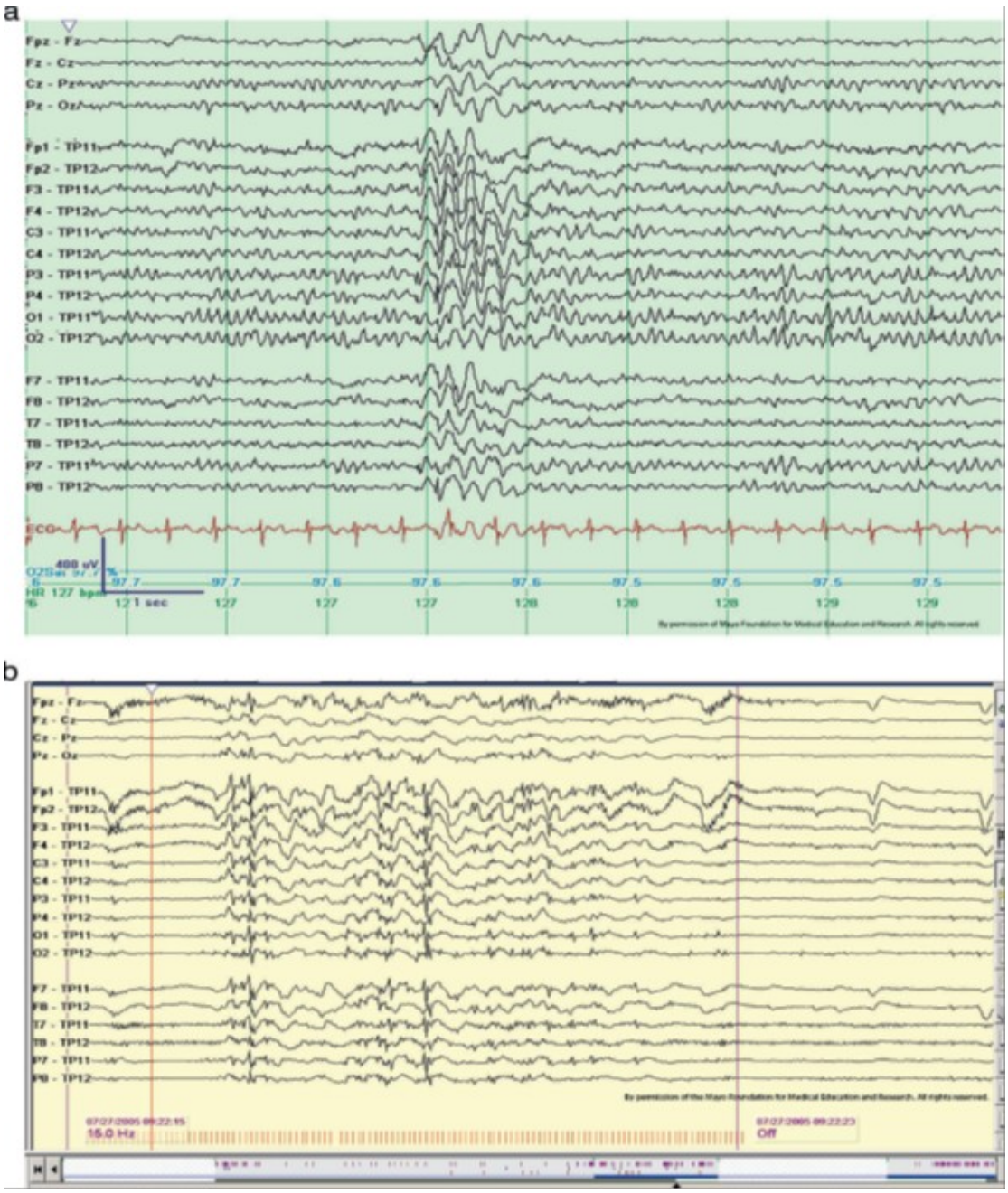
The 10-20 System electrode placements modified for neonates. Most of the neonatal EEG activity is found in the central regions of the brain, therefore the neonatal montage should have sufficient coverage of the centro-temporal regions. Figure courtesy of Elia M. Pestana- Knight, MD, Cleveland Clinic Foundation.



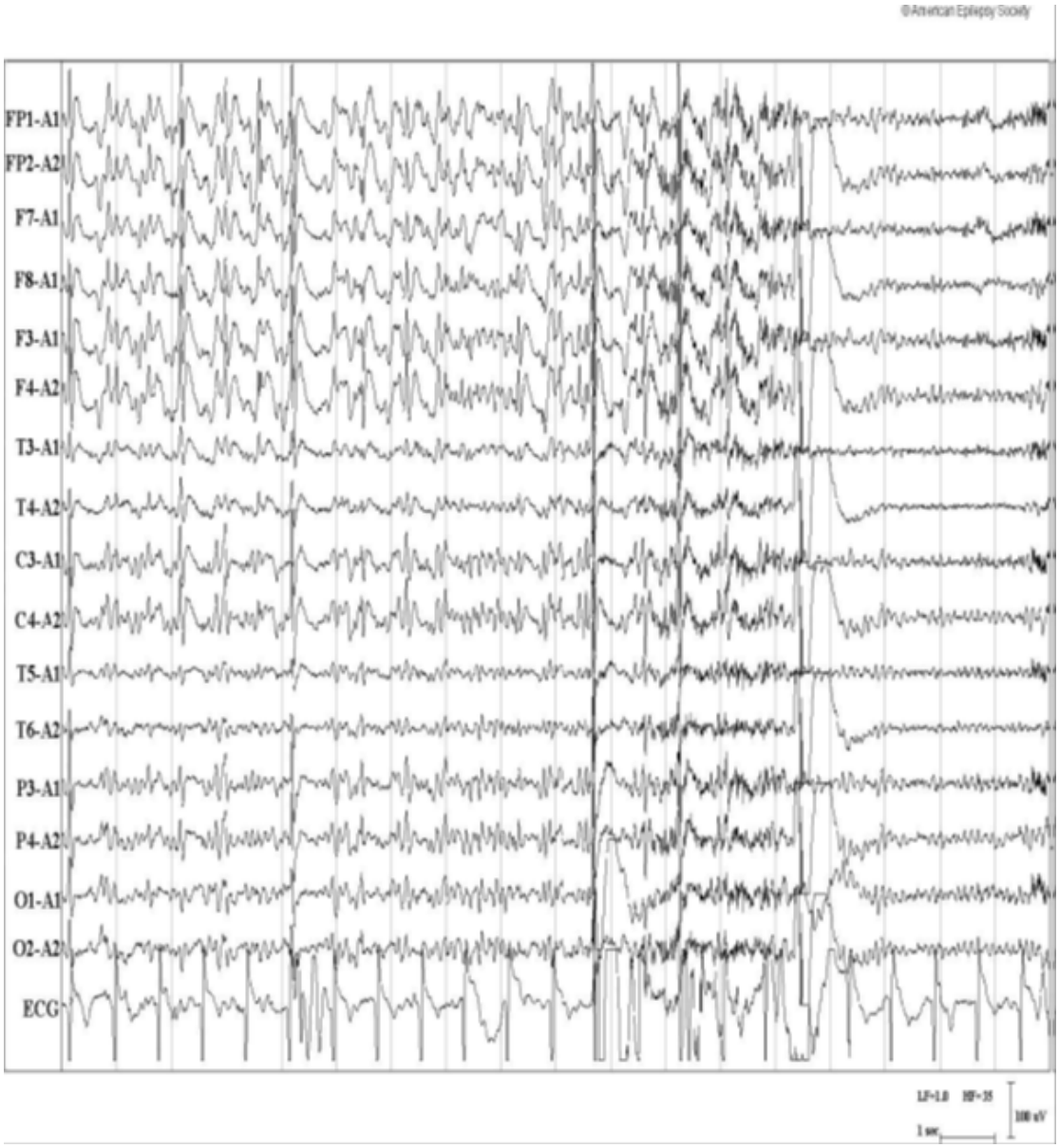
The 3-Hz (typical) generalized spike-wave IED. This IED is most commonly seen in children with childhood absence seizures.



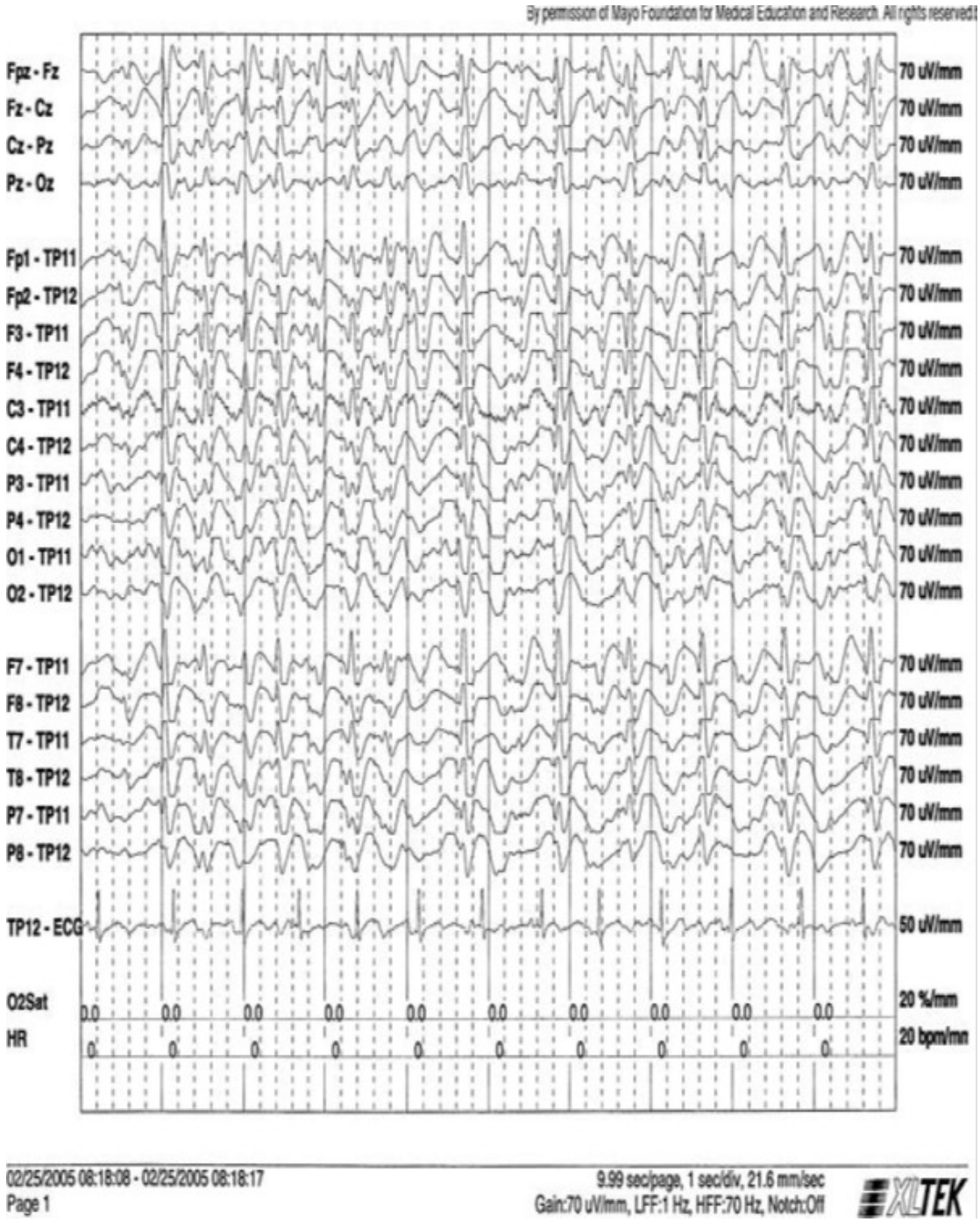
EEG the pattern shown here is temporal intermittent rhythmic delta activity (TIRDA), seen in temporal lobe epilepsy.



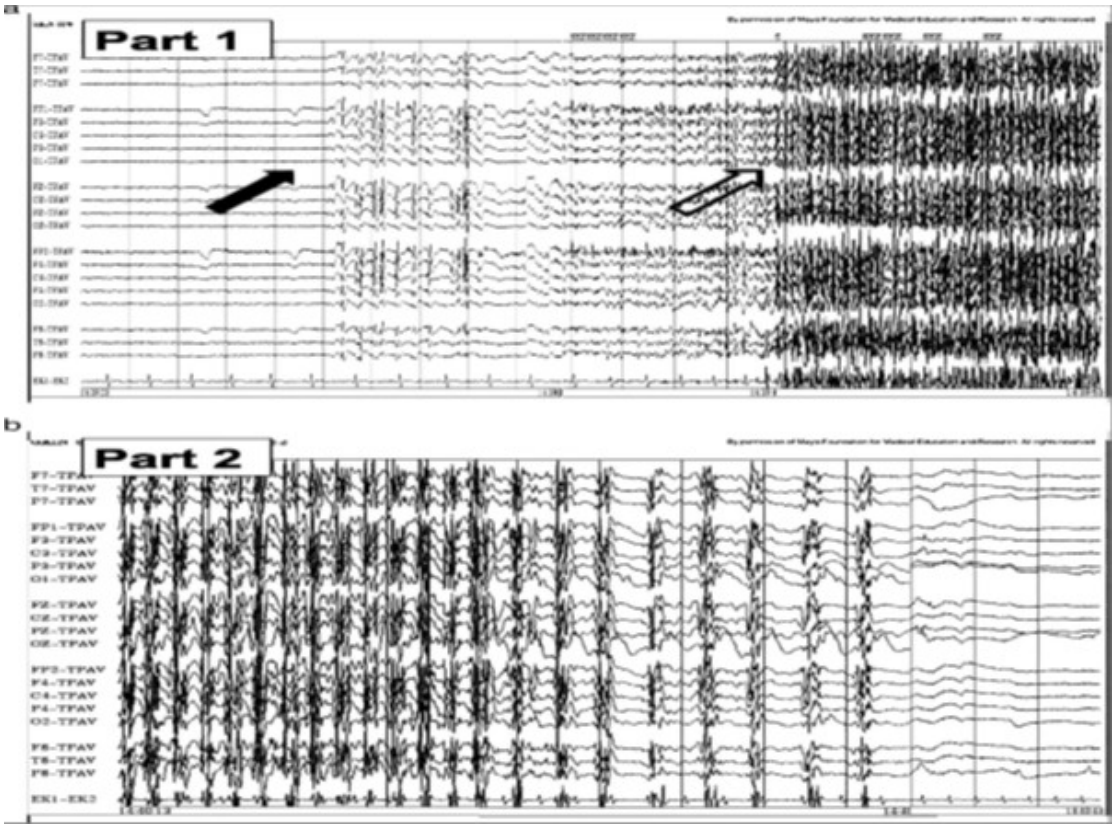
Atypical generalized spike-wave IED. This IED is most commonly seen in children with juvenile absence or myoclonic epilepsy syndrome myoclonic epilepsy syndromes.



Myoclonic seizure in a patient with JME. The patient had a generalized axial myoclonic jerk during second 14, which coincided with the generalized spike-wave discharge and electro decremental pattern seen on EEG.



Slow spike-wave IED typical of the Lennox-Gastaut syndrome. Also note the associated underlying background slowing, indicative of generalized cerebral dysfunction and an epileptic encephalopathy.



Part 1 shows the onset of generalized tonic-clonic seizure in the longitudinal average ear referential montage. Generalized spike and wave and polyspikes are noted at seizure onset (filled arrow), evolving to continuous activation of spike-wave discharges largely obscured by muscle and movement artefact during the tonic phase (open arrow). (b) Part 2 shows the seizure progressing to the clonic phase, with intermittent bursts of diffuse high-frequency activity and progressively longer intervals of suppression between bursts, which parallel the slowing of the clonic clinical jerking movements. The postictal phase follows seizure termination and is marked by diffuse suppression as noted in the latter portion of the epoch shown.

Left temporal onset seizure. The left temporal lobe onset seizure discharge with onset shows rhythmic delta localized to the left anterior temporal region, with phase-reversal noted over the F7-T7 and F9-T9 derivations (filled arrow). Discharge evolves into rhythmic left temporal theta (open arrow) toward the end of the epoch shown.

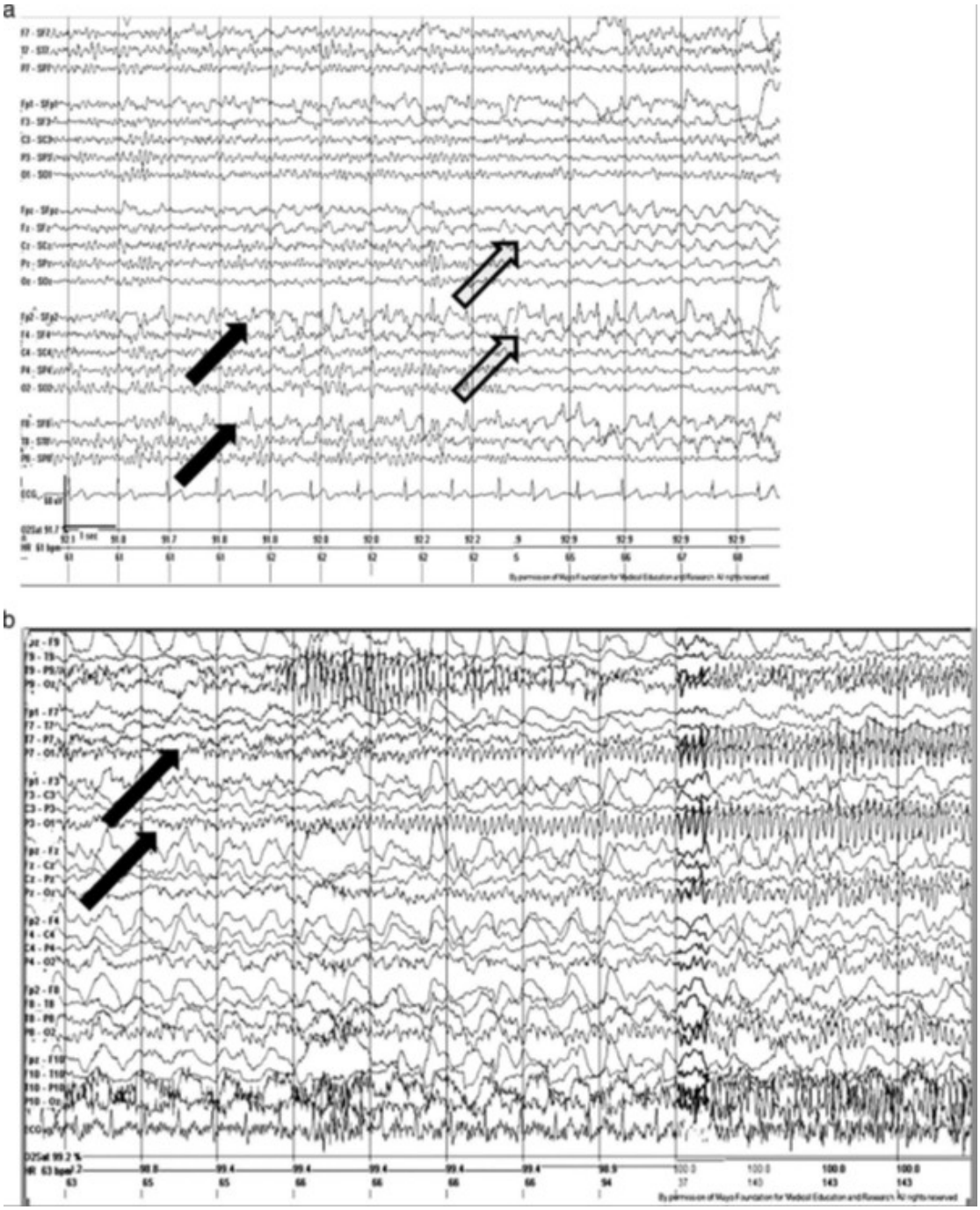


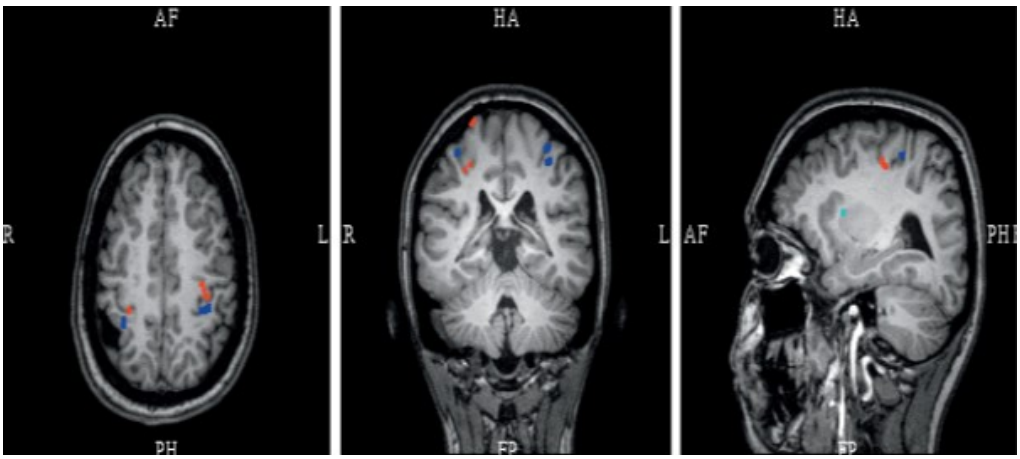
Figure shows extratemporal seizures

Frontal lobe seizures occipital lobe seizures

MAGNETOENCEPHALOGRAPHY

Magnetoencephalography (MEG) measures the small magnetic fields that are generated during seizure activity.it is another way of looking cortical activity non-invasively. MEG records epileptiform activity which can be analysed by various mathematical formula to find its source in the brain. These sources are plotted on anatomic image of brain such as MRI and a magnetic source image is generated using MSI are also used to localize potential seizure foci.

Example of MEG. Equivalent current dipoles in a young girl with tuberous sclerosis. Color-coded regions of interest represent hand motor (red), somatosensory (blue), and epileptiform dipoles (aqua). The sagittal image demonstrates that epileptiform dipoles neighbour a structural tuber and are distant from motor and somatosensory functions.



BRAIN IMAGING

Brain imaging should be done for all the patient who have new onset seizure to search for any structural abnormality that is responsible for seizures. In children who have an unambiguous clinical history and physical examination which suggestive of a benign, generalized seizure disorder such as absence seizure are only exception to this rule.

MRI brain is found to be superior to CT brain in diagnosis of for cerebral lesions associated with seizure disorder. MRI brain useful in identify lesions such as vascular malformations, cerebral tumours or other pathologies that warrants immediate therapy. The newer MRI methods such as 3-tesla scanners, multichannel head Coils, three-dimensional structural imaging at submillimetre resolution, and new pulse sequences including fluid-attenuated inversion Recovery (flair) imaging, has higher sensitivity for detection of structural abnormalities of cortical architecture such as hippocampal atrophy as seen in mesial temporal sclerosis, as well as other cortical neuronal migration abnormalities.

CT brain is preferred in case of emergency such as suspected CNS infection, mass lesion where MRI is not immediately available.MRI study can be done within few days. Other imaging helpful in diagnosis of seizure include functional imaging procedures such as positron

emission tomography (pet) and single-photon emission computed tomography (SPECT).

TREATMENT

Treatment of a patient with a seizure disorder is almost always multimodal.

It includes

1) Treatment of underlying conditions that cause or contribute to the seizures

2) Avoidance of precipitating factors

3) Antileptic drug therapy and suppression of recurrent seizures by prophylactic therapy with antiepileptic medications or surgery.

4) Addressing a variety of psychological and social issues.

When to Start Antileptic Therapy

antiepileptic drug therapy should be started in all the patient who presented with recurrent seizure of unknown aetiology or a known cause that cannot be treated by other modalities such as surgery.

Whether to initiate therapy in a patient with a single seizure is controversial. If patient have risk for recurrent seizure should have been treated.

Risk factors associated with recurrent seizures include the following:

1) An abnormal central nervous system examination

2) Status epilepticus,

3) Postictal Todd's paralysis

4) A strong positive family history of seizures

5) An abnormal EEG.

Most patients with one or more of these risk factors should be treated.

A patient with a single, idiopathic seizure episode whose job depends on driving should be started on antileptic drugs rather risk a seizure prefer taking

Recurrence and the potential loss of driving privileges.

SELECTION OF ANTILEPTIC DRUGS

Generalised Tonic-Clonic Seizures

First line drugs

1) Valproate

2) Lamotrigine

3) Topiramate

Second line drugs

1) Phenytoin
2) Carbamazepine
3) Oxcarbamazepine
4) Phenobarbital
5) Primidone
6) Felbamate
7) Zonisamide

FOCAL SEIZURES

First line drugs

1) Lamotrigine
2) Carbamazepine
3) Oxcarbamazepine
4) Phenytoin
5) Levetiracetam

Alternative Drugs

1) Topiramate
2) Zonisamide
3) Valproic acid
4) Tiagabine
5) Gabapentin

6) Lacosamide

7) Phenobarbital

8) Primidone

9) Felbamate

TYPICAL ABSENCE SEIZURE

First line drugs

1) Valproic acid

2) Ethosuximide

Alternative Drugs

1) Lamotrigine

2) Clonazepam

ATYPICAL ABSENCE, MYOCLONIC, ATONIC SEIZURES

First Line Drugs

1) Valproic acid

2) Lamotrigine

3) Topiramate

Alternative drugs

1) Clonazepam

2) Felbamate

DRUGS DOSAGE AND SIDE EFFECTS

1.Phenytoin

Dose: 300-400mg/d; qd-bid

Therapeutic range: 10-20mcg/ml

Adverse Effect

Neurologic	Systemic
Dizziness	Gum hyperplasia
Diplopia	Lymphadenopathy
Ataxia	Hirsutism
Incoordination	Osteomalacia
Confusion	Facial coarsening
	Skin rash

2.Carbamazepine

Dose:600-800; bid-qid

Therapeutic range:6-12mcg/ml

Adverse Effects

Neurologic	Systemic
Ataxia	Aplastic anaemia
Dizziness	Leukopenia
Diplopia	Gastrointestinal irritation
	Hepatotoxicity
	Hyponatremia

Valproic Acid

Dose:750-2000mg/d; bid-qid

Therapeutic range:50-125mcg/ml

Adverse Effects

Neurologic	Systemic
Ataxia Tremor Sedation	Hepatotoxicity Thrombocytopenia Gastrointestinal irritation Weight gain Transient alopecia Hyperammonaemia

Lamotrigine

Dose:150-500mg/d; bid

Therapeutic range: not established

Adverse Effects

Neurologic side effects	Systemic
Dizziness Diplopia Ataxia headache	Skin rash Steven- Johnson syndrome

Ethosuximide

Dose:750-1250mg/d; qd-bid

Therapeutic range:40-100mcg/ml

Adverse Effects

Neurologic:	**Systemic:**
Ataxia Headache	Bone marrow suppression Skin rash GI irritation

Gabapentin:

Dose:900-2400mg/d; tid-qid

Therapeutic range: not established

Adverse Effects

Neurologic	**Systemic**
Ataxia Sedation	Weight gain GI irritation Edema

Topiramate

Dose:200-400mg/d; bid

Therapeutic range: not established

Adverse Effects

Neurologic	**Systemic**
Psychomotor slowing Speech or language problems paraesthesia's	Renal stones Glaucoma Weight loss hyperhidrosis

Phenobarbital

Dose:60-180mg/d; qd

Therapeutic range:10-40mg/ml

Adverse Effects

Neurologic	Systemic
Ataxia Confusion Decrease libido Depression	Skin rash

Clonazepam

Dose:1-12mg/d; qd-tid

Therapeutic range:10-70ng/ml

Adverse Effects

Neurological	Systemic
Ataxia Sedation Lethargy	Anorexia

Tiagabine

Dose:32-56mg/d; bid-qid

Therapeutic range: not established

Adverse Effects

Neurologic	Systemic
Confusion Sedation Depression Paraesthesia Psychosis	Gastrointestinal irritation

Felbamate

Dose:2400-3600 mg/d; bid-qid

Therapeutic range: not established

Adverse Effects

Neurologic	Systemic
Insomnia	Aplastic anaemia
Dizziness	Hepatic failure
Sedation	Weight loss
Headache	Gastrointestinal irritation

Levetiracetam

Dose:1000-3000mg/d; qd-bid

Therapeutic range: not established

Adverse Effects

Neurologic	Systemic
Sedation	Anaemia
Fatigue	Leukopenia
Incoordination	
Mood changes	

Zonisamide

Dose:200-400mg/d; qd-bid

Therapeutic range:

Adverse Effects

Neurologic	Systemic
Sedation	Anorexia
Dizziness	Renal stones
Confusion	Hyperhidrosis
Headache	
Psychosis	

Oxcarbazepine

Dose:900-2400; qd-bid

Therapeutic range: not established

Adverse Effects

Neurologic	Systemic
Fatigue	Aplastic anaemia
Ataxia	Leukopenia
Diplopia	Hepatotoxicity
Vertigo	Hyponatremia

Lacosamide

Dose:200-400mg/d; bid

Therapeutic range: not established

Adverse Effects

Neurologic	Systemic
Dizziness	GI irritation
Ataxia	PR interval prolongation
Diplopia	
Vertigo	

Rufinamide

Dose:3200mg/d; bid

Therapeutic range: not established

Adverse Effects

Neurologic	Systemic
Sedation	GI irritation
Fatigue	Leukopenia
Dizziness	QT prolongation
Ataxia	
Headache	
Diplopia	

SURGICAL TREATMENT OF REFRACTORY EPILEPSY

Approximately 20–30% of patients with epilepsy continue to have seizures despite efforts to find an effective combination of antiepileptic drugs. For some, surgery can be extremely effective in substantially reducing seizure frequency and even providing complete seizure control. understanding the potential value of surgery is especially important when a patient's seizures are not controlled with initial treatment, as such patients often fail to respond to subsequent medication trials. Rather than submitting the patient to years of unsuccessful medical therapy and the psychosocial trauma and increased mortality associated with ongoing seizures, the patient should have an efficient but relatively brief attempt at medical therapy and then be referred for surgical evaluation.

The most common surgical procedure for patients with temporal lobe epilepsy involves resection of the anteromedial temporal lobe (temporal lobectomy) or a more limited removal of the underlying hippocampus and amygdala (amygdalohippocampectomy).

Focal seizures arising from extratemporal regions may be abolished by a focal neocortical resection with precise removal of an identified lesion (lesionectomy). When the cortical region cannot be removed, multiple subpial transection, which disrupts intracortical connections, is sometimes used to prevent seizure spread.

Hemispherectomy or multilobar resection is useful for some patients with severe seizures due to hemispheric abnormalities such as hemimegalencephaly or other dysplastic abnormalities, and corpus callosotomy has been shown to be effective for disabling tonic or atonic seizures, usually when they are part of a mixed-seizure syndrome (e.g., Lennox-Gastaut syndrome).

Presurgical evaluation is designed to identify the functional and structural basis of the patient's seizure disorder. Inpatient video-EEG monitoring is used to define the anatomic location of the seizure focus and to correlate the abnormal electrophysiologic activity with behavioral manifestations of the seizure. Routine scalp or scalp-sphenoidal recordings are usually sufficient for localization, and advances in neuroimaging have made the use of invasive electrophysiologic monitoring such as implanted depth electrodes or subdural electrodes less common. A high-resolution MRI scan is routinely used to identify structural lesions, and this is sometimes augmented with MEG. Functional imaging studies such as SPECT and PET are adjunctive tests that may help verify the localization of an apparent epileptogenic region. Once the presumed location of the seizure onset is identified, additional studies, including neuropsychological testing and the intracarotid amobarbital test (Wada test) may be used to assess language and memory localization and to determine the possible functional consequences of surgical removal of the epileptogenic region. In some

cases, the exact extent of the resection to be undertaken is determined by performing cortical mapping at the time of the surgical procedure, allowing for a tailored resection. This involves electrocorticographic recordings made with electrodes on the surface of the brain to identify the extent of epileptiform disturbances. If the region to be resected is within or near brain regions suspected of having sensorimotor or language function, electrical cortical stimulation mapping is performed on the awake patient to determine the function of cortical regions in question in order to avoid resection of so-called eloquent cortex and thereby minimize postsurgical deficits.

Advances in presurgical evaluation and microsurgical techniques have led to a steady increase in the success of epilepsy surgery. Clinically significant complications of surgery are <5%, and the use of functional mapping procedures has markedly reduced the neurologic sequelae due to removal or sectioning of brain tissue. For example, about 70% of patients treated with temporal lobectomy will become seizure free, and another 15–25% will have at least a 90% reduction in seizure frequency. Marked improvement is also usually seen in patients treated with hemispherectomy for catastrophic seizure disorders due to large hemispheric abnormalities. Postoperatively, patients generally need to remain on antiepileptic drug therapy, but the marked reduction of seizures following resective surgery can have a very beneficial effect on quality of life. Not all medically refractory patients are suitable

candidates for resective surgery. For example, some patients have seizures arising from more than one site, making the risk of ongoing seizures or potential harm from the surgery unacceptably high.

Vagus nerve stimulation (VNS) may be useful in some of these cases, although the benefit for most patients seems to be very limited (i.e., the efficacy of VNS appears to be no greater than trying another drug, which rarely works if a patient has proved to be refractory to the first two to three drugs). The precise mechanism of action of VNS is unknown, although experimental studies have shown that stimulation of vagal nuclei leads to widespread activation of cortical and subcortical pathways and an associated increased seizure threshold. Adverse effects of the surgery are rare, and stimulation-induced side effects, including transient hoarseness, cough, and dyspnoea, are usually mild. Although still in development, there are some additional therapies that will likely be of benefit to patients with medically refractory epilepsy. Preliminary studies suggest that stereotactic radiosurgery may be effective in certain focal seizure disorders.

There has also been great interest in the development of implantable devices that can detect the onset of a seizure (in some instances, before the seizure becomes clinically apparent) and deliver either an electrical stimulation or drug directly to the Seizure focus to abort the event.

PROLACTIN

PRL consists of 198 amino acids and has a molecular mass of 21,500 kDa; it is weakly homologous to GH and human placental lactogen (hPL), reflecting the duplication and divergence of a common GH-PRL-hPL precursor gene. PRL is synthesized in lactotropes, which constitute about 20% of anterior pituitary cells. Lactotropes and somatotropes are derived from a common precursor cell that may give rise to a tumour that secretes both PRL and GH. Marked lactotrope cell hyperplasia develops during pregnancy and the first few months of lactation. These transient functional changes in the lactotrope population are induced by estrogen.

SECRETION

Normal adult serum PRL levels are about 10–25 μg/L in women and 10–20 μg/L in men. PRL secretion is pulsatile, with the highest secretory peaks occurring during rapid eye movement sleep. Peak serum PRL levels (up to 30 μg/L) occur between 4:00 and 6:00 a.m. The circulating half-life of PRL is about 50 min. PRL is unique among the pituitary hormones in that the predominant central control mechanism is inhibitory, reflecting dopamine mediated suppression of PRL release. This regulatory pathway accounts for the spontaneous PRL hypersecretion that occurs with Pituitary stalk section, often a consequence of compressive mass lesions at the skull base.

Pituitary dopamine type 2 (D 2) receptors mediate inhibition of PRL synthesis and secretion. Targeted disruption (gene knockout) of the murine D 2 receptor in mice results in hyperprolactinemia and lactotrope proliferation. As discussed below, dopamine agonists play a central role in the management of hyperprolactinaemic disorders.

Thyrotropin-releasing hormone (TRH) (pyro Glu-His-Pro-NH2) is a hypothalamic tripeptide that elicits prolactin release within 15–30 min after intravenous injection. The physiologic relevance of TRH for PRL regulation is unclear, and it appears primarily to regulate TSH. Vasoactive intestinal peptide (VIP) also induces PRL release, whereas glucocorticoids and thyroid hormone weakly suppress PRL secretion.

Serum PRL levels rise transiently after exercise, meals, sexual intercourse, minor surgical procedures, general anaesthesia, chest wall injury, acute myocardial infarction, and other forms of acute stress.

PRL levels increase markedly (about tenfold) during pregnancy and decline rapidly within 2 weeks of parturition. If breast-feeding is initiated, basal PRL levels remain elevated; suckling stimulates reflex increases in PRL levels that last for about 30–45 min. Breast suckling activates neural afferent pathways in the hypothalamus that induce PRL release. With time, suckling-induced responses diminish and interfeeding PRL levels return to normal.

ACTION

The PRL receptor is a member of the type I cytokine receptor family that also includes GH and interleukin (IL) 6 receptors. Ligand binding induces receptor dimerization and intracellular signalling by Janus kinase (jak), which stimulates translocation of the signal transduction and activators of transcription (stat) family to activate target genes. In the breast, the lobuloalveolar epithelium proliferates in response to PRL, placental lactogens, estrogen, progesterone, and local paracrine growth factors, including IGF-I. PRL acts to induce and maintain lactation, decrease reproductive function, and suppress sexual drive. These functions are geared toward ensuring that maternal lactation is sustained and not interrupted by pregnancy.

PRL inhibits reproductive function by suppressing hypothalamic GNRH and pituitary Gonadotropin secretion and by impairing gonadal steroidogenesis in both women and men. In the ovary, PRL blocks folliculogenesis and inhibits granulosa cell aromatase activity, leading to hypoestrogenism and anovulation.

PRL also has a luteolytic effect, generating a shortened, or inadequate, luteal phase of the menstrual cycle. In men, attenuated LH secretion leads to low testosterone levels and decreased spermatogenesis. These hormonal changes decrease libido and reduce fertility in patients with hyperprolactinemia.

AIMS AND OBJECTIVES:

The aim of the study to study the clinical & biochemical correlation in various types of seizures and Pseudoseizure

PRIMARY OBJECTIVES

To differentiate seizures from pseudo seizure using serum prolactin

SECONDARY OBJECTIVES

To correlate different types of seizures with biochemical parameters such as random blood sugar, & serum electrolytes

MATERIALS AND METHODS

STUDY SETTING

Patient admitted in medicine & neuromedicne department of government Stanley Medical College from APRIL 2018 to SEPTEMBER 2018.

ETHICAL APPROVAL

Institutional ethics committee approval was obtained to conduct the study.

STUDY GROUP

All patient who were admitted with episode of seizure in medicine and neuromedicine ward from April 2018 to September 2018.

STUDY DESIGN

Prospective descriptive study.

POPULATION STUDIED

115

DURATION OF STUDY

6 months (APRIL 2018 – SEPTEMBER 2018)

CONSENT

Written informed consent were obtained from all patients

INCLUSTION CRITERIA

Patients admitted with new onset seizures from age group 15-70yrs of age

EXCLUSION CRITERIA

- Patients admitted with head injury
- Lactating and pregnant women
- Patients with chronic kidney disease, hypothyroidism and decompensated liver disease
- Patients taking drugs atypical antipsychotics such as clozapine ,olanzapine,risperidone,quetiapine,chlorpromazine,haloperidol,metoclopramide, alpha methyl dopa,imipramine,serotonin reuptake inhibitors and verapamil
- Patients with pituitary adenoma and acromegaly

PROTOCOL OF THE STUDY

- Patient admitted with history of seizure from age group 15-60yr
- For every case selected, detailed clinical history rule out pseudo seizures and associated comorbid illnesses like diabetes mellitus, systemic hypertension, hyperlipidaemia, bronchial asthma, chronic kidney disease, psychiatric illness family history of diabetes mellitus, seizures, psychiatric illness and drug history are obtained.

- In all cases, blood for baseline investigation such as renal function test, serum electrolyte, serum prolactin at 30 min and 2hr after seizure episode are done by performing venepuncture and estimation will be done biochemical laboratory, biochemical department at govt. Stanley medical college.

- For all these patients EEG were done and classified into two groups based on both clinical history and EEG finding

- Blood investigation is such as random blood sugar, serum electrolyte, serum sodium, and EEG were compared between two groups.

    - Normal prolactin levels

      Males - 10-20mcgu/l

      Females – 10 – 25 mcgU/l

- Values twice baseline level or greater 36mcgu/l are considered as elevated

The following investigations were done to all patients included in the study:

- Serum prolactin
- Serum electrolytes
- Renal function test
- Random blood sugar
- Electroencephalogram

CONFLICT OF INTEREST:

None

DATA ANALYSIS

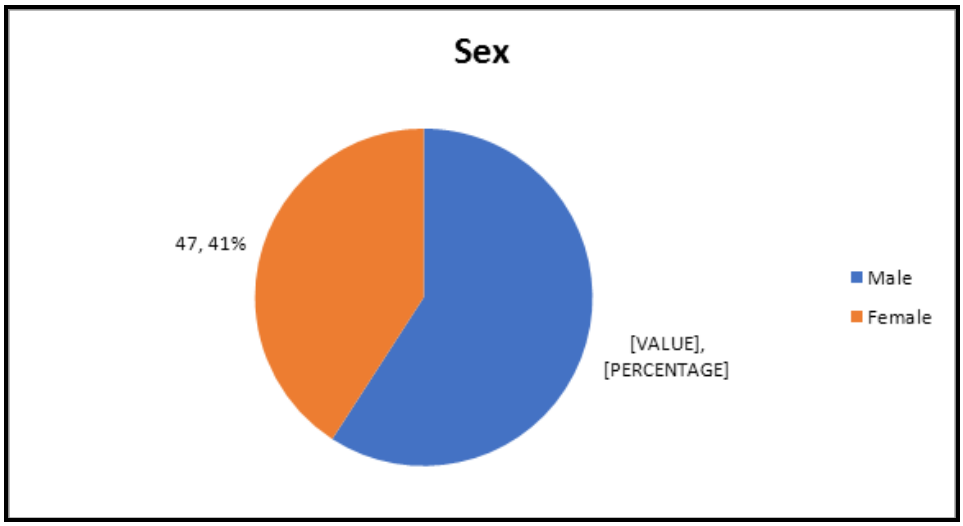
The collected data were analysed using IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics, percentage analysis, frequency analysis was used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the bivariate samples in The Independent groups the Unpaired sample t-test was used. To find the significance in categorical data Chi-Square test was used similarly if the expected cell frequency is less than 5 in 2×2 tables then the Fisher's Exact was used. In all the above mentioned statistical tools the probability value .05 is considered as significant level.

P - Value	** Highly Significant at P ≤ .01
P -Value	# No Significant at P >.05

POPULATION CHARACTERISTIC

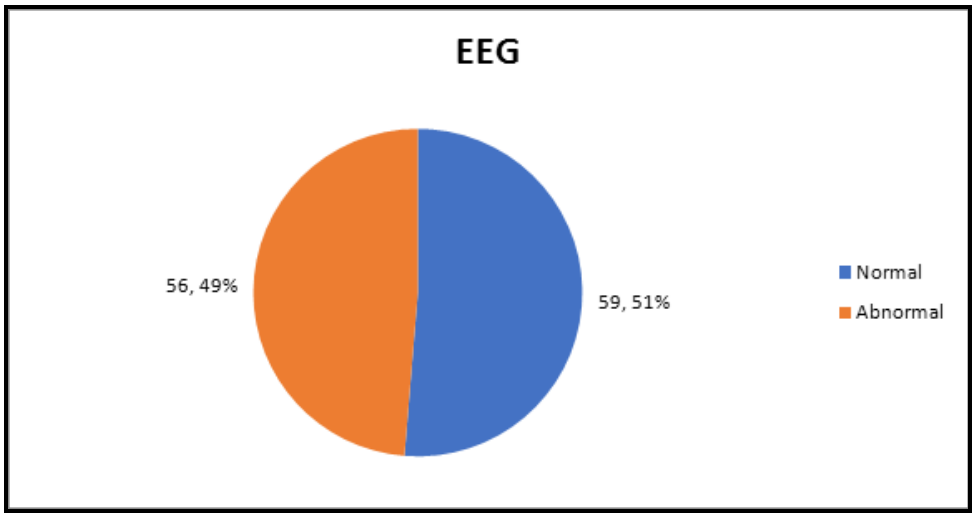
The study population contain 115 patients of which 61 patients classified into seizure group and 54 patient belongs to pseudo seizure group. 68 patients are male and 47 patients are female

Fig-1



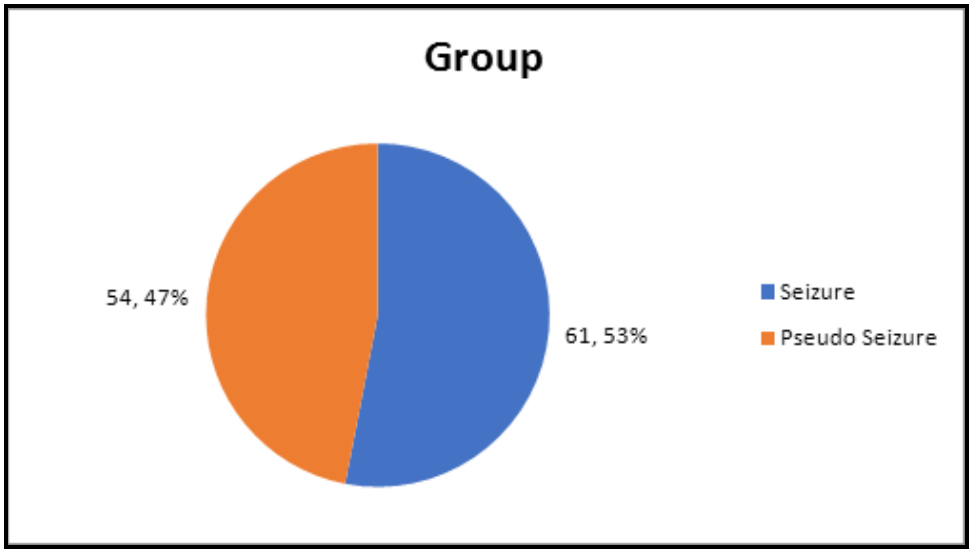
This pie chart shows male female distribution of study patients of 115 patient studied 68 patients are male and 47 patients are female i.e. 59% of the people are male and 41% are female.

Fig-2



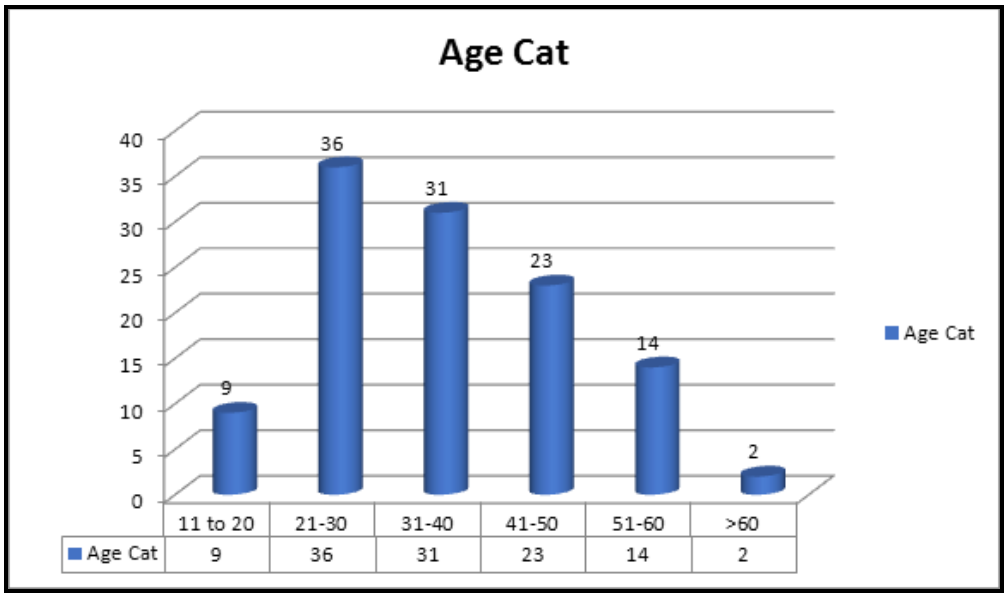
This pie chart shows distribution of normal and abnormal EEG among study population. Of those 115 patients studied 59 patient showed normal EEG study and 56 patients showed abnormal study.i.e. 51% of patient with normal EEG study and 49% of patient with abnormal EEG study.

Fig-3



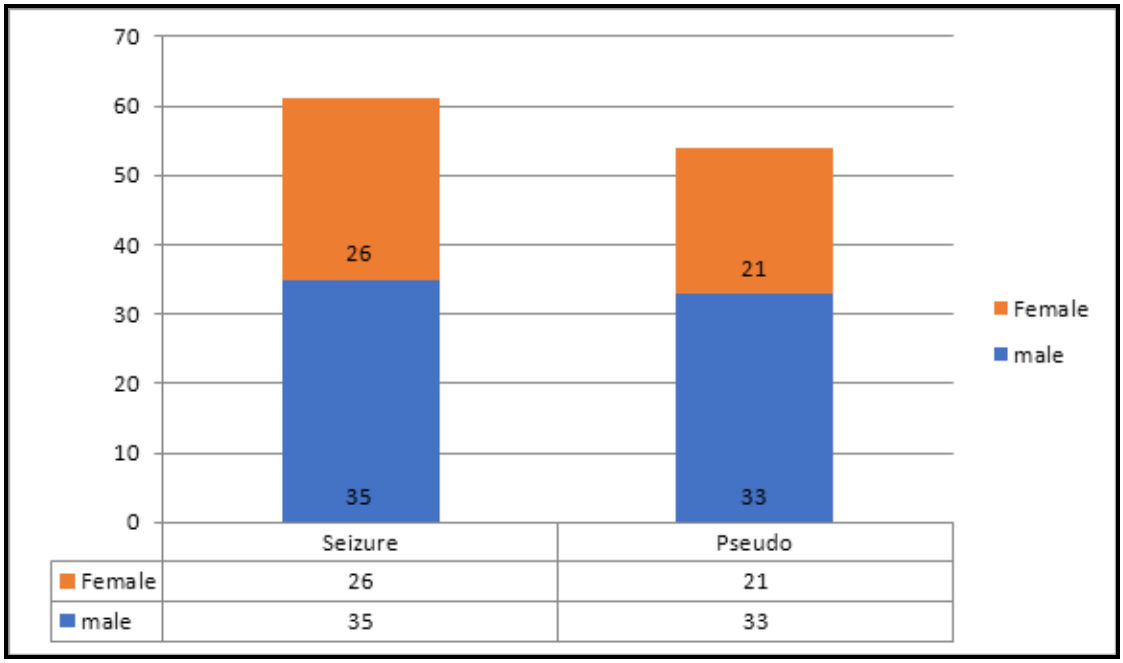
This pie chart shows distribution among seizure and pseudo seizure group. 61 patients belong to seizure group and 54 patients belong to pseudo seizure group i.e. 53% belong to seizure group and 47% belongs to pseudo seizure group.

Fig-4



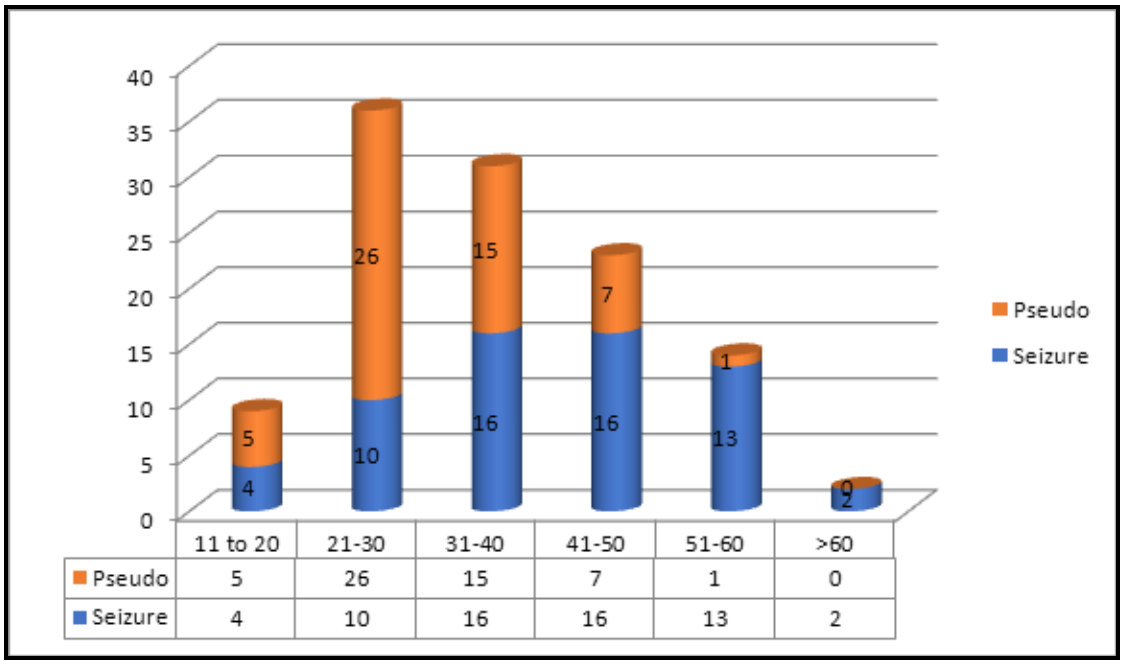
This bar diagram shows age wise distribution of study population. 11- 20yrs: 9, 21-30yrs:36, 31-40yrs: 31, 41-50yrs:23, 51-60yrs:14, >60yrs:2.

Fig-5



This bar diagram shows distribution of male and female patients among seizure and pseudo seizure group. Among seizure group 35 patients are male and 26 patients are female. In pseudo seizure group 33 patients are male and 21 patients are female.

Fig-6



This bar diagram shows age wise distribution among seizure and pseudo seizure group. Among age group of 11 to 20yrs, four patients belong to seizure group and five patients belong to pseudo seizure group. Among age group of 21-30yrs, 26 patients belong to pseudo seizure group and 10patients belongs to seizure. Among age group31-40yrs,15 patients belong to pseudo seizure group and 16 patients belongs to seizure group. Among age group41- 50yrs, 7 patients belong to pseudo seizure group and sixteen patients belongs to seizure group. Among age group 51-60yrs, one patient belongs to Pseudoseizure group and 13 patients belong to seizure group. Among age more than 60yrs only two patients belong to seizure group.

Table-1

AGE	
Mean	35.63
Median	35.00
Std. Deviation	12.010
Minimum	16
Maximum	65

Mean age of study population is 35.63. median is 35, standard deviation is 12.010.

Table-2: Gender Distribution

Sex	Frequency	Percent
Male	68	59.1
Female	47	40.9
Total	115	100.0

Table-3: EEG findings in my study subjects

EEG		Frequency	Percent
Valid	Normal	59	51.3
	Abnormal	56	48.7
	Total	115	100.0

Table-4

Group	Frequency	Percent
Seizure	61	53
Pseudo seizure	54	47
Total	115	100.0

Table-5: Age wise distribution of study subjects

Age Cat		Frequency	Percent
Valid	11-20	9	7.8
	21-30	36	31.3
	31-40	31	27.0
	41-50	23	20.0
	51-60	14	12.2
	>60	2	1.7
	Total	115	100.0

Table-6

SEIZURE TYPE	MALE	FEMALE
GTCS	21	17
FOCAL	12	8
ABSENCE	1	1
MYOGENIC	1	0

Table-7: Biochemical correlation of my study subjects between seizure and pseudo seizure

Group Statistics					
	V9	**N**	**Mean**	**Std. Deviation**	**P value**
S. PROLAC30	1.00	61	47.43	12.467	
	2.00	54	16.83	8.325	0.001*
S.P @ 2 hr	1.00	61	41.05	11.442	0.001*
	2.00	54	13.31	3.680	
RBS	1.00	61	164.46	126.638	0.01*
	2.00	54	118.22	43.029	
NA	1.00	61	133.26	26.139	0.51
	2.00	54	135.89	14.699	

*significant, "Unpaired t test "

In my study mean value of s. prolactin at 30 min is 47.43for seizure group and 16.83 for pseudo seizure group. And SD for seizure group is 12.467, Pseudoseizure group is 8.325 and p value is 0.001 which is statistically significant using unpaired t test.

Mean value for s. prolactin at 2hr is 41.05 for seizure group and 13.31 for pseudo seizure group.SD seizure group is 11.442 and pseudo seizure group is 3.680.p value is 0.001 using unpaired t test which is statistically significant.

Mean value for random blood sugar is 164.46 for seizure group. And pseudo seizure group is 118. p value is 0.01.

Mean value of sodium in seizure group is 133.26 and for pseudo seizure group is 135.89. p value is 0.51.

Table-8

Crosstab count				
Group	**Sexnew**		**Total**	**P value ***
	Male	**Female**		**Df=1**
Seizure	35	26	61	0.683
Pseudoseizure	33	21	54	
Total	68	47	115	

*Chi square test.

P value for cross tab count is 0.683 and is statistically not significant.

Table-9: Gender wise clinical correlation among my study subjects

Crosstab				
Count				
EEG	Sexnew		Total	Value *
	Male	Female		Df=1
Normal	36	23	59	0.67
Abnormal	32	24	56	
Total	68	47	115	

*Chi square test

P value for gender wise EEG correlation is 0.67 which is not significant.

Table-10: Clinical correlation between seizure group and non-seizure group

Count				
EEG	Group		Total	P value
	Seizure	Pseudo		Df=1
Normal	5	54	59	
abnormal	56	0	56	0.001
Total	61	54	115	

P value EEG correlation between seizure and Pseudoseizure group is 0.001.

Table-11

Age	Group		Total	P value
	Seizure	Pseudo		Df=5
11-20	4	5	9	
21-30	10	26	36	
31-40	16	15	31	
41-50	16	7	23	0.001
51-60	13	1	14	
>60	2	0	2	
Total	61	54	115	

P value for age wise correlation between seizure and pseudo seizure group is 0.001

Prolactin levels in Males

Variable	Frequency	Percent	Frequency	Percent
S. Prolactin	**At 30 min**		**At 2 Hr**	
Normal	30	44.1	37	54.4
Abnormal	38	55.9	31	45.6
Total	68	100.0	68	100.0

Prolactin level in Females

Variable	Frequency	Percent	Frequency	Percent
S. Prolactin	**At 30 min**		**At 2 Hr**	
Normal	20	42.6	25	46.8
Abnormal	27	57.4	22	53.2
Total	47	100.0	47	100.0

DISCUSSION

- This study consists of 115 patients in age groups from 15yrs to 60 years with new onset seizures admitted in a Tertiary care hospital. The study was conducted from April 2018-September 2018.

- Among 115 patients were studied 61 patients were classified into seizure group based on clinical history and positive EEG findings and 54 patients are classified into Pseudoseizure group.

- Among the study groups (n=115), males (59.1%) are more commonly affected with seizures than females (40.1%)

- The mean age of the study group is 35.63 The age group affected more is from 20-40 years contributing about 58.3% of the study population

- Among 61 patients in seizure group, 59 patients had shown positive EEG changes during postictal period.in other patients EEG findings were normal

- Serum prolactin levels is found to be elevated at both 30 min and 2hr after seizure in seizure group and is normal at both 30 min and 2hr in pseudo seizure group and statistical analysis shows significant difference in the two groups.

- Random blood sugar is lower for pseudo seizure group when compared to seizure group and statistical analysis shows difference is significant.

- There is no significant difference in serum sodium among seizure and pseudo seizure group.

CONCLUSION

- The following were the conclusion of this study
- Males were more commonly affected
- General clonic tonic seizure was most common seizure type
- EEG was most useful in differentiating seizures and pseudoseizures when it was done in ictal or postictal period
- Serum prolactin were useful in differentiating seizure and Pseudoseizure.

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PROFORMA

NAME : AGE: SEX:

ADDRESS: CONTACT NO:

COMPLAINTS:

HISTORY

ALCOHOLISM	YES	NO
DURATION		
HEAD INJURY	YES	NO
DIABETES MELLITUS	YES	NO
HYPERTENSION	YES	NO
CHRONIC KIDNEY DIASEASE	YES	NO
LIVER DISEASE	YES	NO
HYPOTHYROIDISM	YES	NO
SEIZURE DISORDER	YES	NO
SMOKER	YES	NO
PSYCHIATRIC ILLNESS	YES	NO

H/O MEDICATION -

RELEVANT CLINICAL EXAMINATION:

GENERAL EXAMINATION

SYSTEMIC EXAMINATION:

CARDIOVASCULAR:

RESPIRATORY:

ABDOMEN:

CNS:

LABORATORY INVESTIGATION:

RBS: RFT:

SERUM PROLACTIN:

S. ELECTROLYTES:

EEG:

COMMENT:

INFORMED CONSENT

Place of study: Govt. Stanley medical college, Chennai

I …… have been informed about the details of the study in my own language. I have completely understood the details of the study. I am aware of the possible risks and benefits, while taking part in the study. I agree to collect samples of blood, if study needs. I understand that I can withdraw from the study at any point of time and even then, I can receive the medical treatment as usual. I understand that I will not get any money for taking part in the study. I will not object if the results of this study are getting published in any medical journal, provided my personal identity is not revealed. I know what I am supposed to do by taking part in this study and I assure that I would extend my full cooperation for this study.

Volunteer:	Witness:
Name and address:	Name and address:
Signature/thumb impression:	Signature/thumb impression:
Date:	Date:

Investigator Signature and date

INFORMED CONSENT

“A STUDY ON CLINICAL AND BIOCHEMICAL CORRELATION BETWEEN VARIOUS TYPES OF SEIZURES AND PSEUDOSEIZURES

நான் இந்த ஆராய்ச்சியில் விவரங்களை முற்றிலும் புரிந்து கொண்டேன்.

ஆய்வில் பங்கு எடுத்துபோது, சாத்தியமான அபாயங்கள் மற்றும் பயன்களை பற்றி நான் அறிந்துள்ளேன்.

நான் எந்தவொரு வேளையிலும் ஆய்வில் இருந்து திரும்பமுடியும்,அதன்பின்னர், நான் வழக்கம்போல் மருத்துவசிகிச்சை பெறமுடியும் என்று புரிந்து கொள்கிறேன்

நான் ஆய்வில் பங்கு எடுத்து பணம் எதையும் பெறமுடியாது என்று அறிந்துள்ளேன்.

இந்த ஆய்வின் முடிவுகள் எந்த மெடிக்கல்ஜர்னலில் வெளியிடப்பட இருந்தால் நான் எதிர்க்கவில்லை, என் தனிப்பட்ட அடையாளத்தை வெளிப்படுத்தப்பட்டு இருக்ககூடாது.

நான் இந்த ஆய்வில் பங்கெடுப்பதன் மூலம் நான் என்ன செய்யபோகிறேன் என்றுதெரியும்

நான் இந்த ஆய்வில் என் முழுஒத்துழைப்பையும் கொடுப்பேன் என்று உறுதியளிக்கிறேன்.

தன்னார்வளர்	சாட்சி
பெயர்மற்றும்முகவரி	பெயர்மற்றும்முகவரி
கையொப்பம் / விரல்ரேகை:	கையொப்பம் / விரல்ரேகை:

ABBREVATIONS:

EEG	:	ELECTROENCEPHALOGRAM
GTCS	:	GENERALISED TONIC-CLONIC SEIZURE
PS	:	PARTIAL SEIZURE
CPS	:	COMPLEX PARTIAL SEIZURE
PRL	:	PROLACTIN
VIP	:	VASOACTIVE PEPTIDE
TRH	:	THYOTROPIN RELEASING HORMONE
MRI	:	MAGNETIC RESONANCE IMAGING
MEG	:	MAGNETIC ENCEPHALOGRAM
VNS	:	VAGAL NERVE STUDY
S.D	:	STANDARD DEVIATION
CBZ	:	CARABAMAZEPINE
SVP	:	SODIUM VALPORATE

GOVERNMENT STANLEY MEDICAL COLLEGE& HOSPITAL,CHENNAI -01

INSTITUTIONAL ETHICS COMMITTEE

Title of the Work : "A Study Onclinical and Biochemical Correlation Between Various Types of Seizures and Pseudoseizures".

Principal Investigator : DR. S. P. Sridhar,
Designation : PG. MD General Medicine,
Department : Department of General Medicine,
Govt. Stanley Medical College.

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 13.04.2018 at the Council Hall, Stanley Medical College, Chennai-1 at 10am.

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

MEMBER SECRETARY,
IEC, SMC, CHENNAI

MEMBER SECRETARY
ETHICAL COMMITTEE,
STANLEY MEDICAL COLLEGE
CHENNAI-600 001.

MASTER CHART

SL.NO	SEIZURE GROUP							
	NAME	AGE	SEX	EEG N/AB	S.PROLACTIN (mcg/L)		RBS	S.Na+
					30 min	2hr		
1	ESWARI	55	F	AB	51	45	245	132
2	SUSSELA	36	F	AB	46	39	123	136
3	FAZAL	32	M	AB	41	36	109	139
4	ZEENATH BEE	52	F	AB	57	49	88	126
5	VELAYUDAM	65	M	AB	40	32	308	143
6	RENUGA	42	F	AB	53	45	563	124
7	MANNAR	59	M	AB	49	44	254	32
8	PUNITHA	32	F	AB	59	52	123	136
9	PICHAYAMMAL	35	F	AB	62	51	123	39
10	SARALA DEVI	50	F	AB	66	56	112	138
11	PAREMESHWARI	62	M	N	56	49	115	139
12	SHANKAR	35	M	AB	52	42	152	141
13	GEETHA	42	F	AB	47	39	43	128
14	RAJENDRAN	52	M	AB	42	35	128	146
15	SUNDARAM	35	M	AB	61	52	127	135
16	VATCHALA	40	F	AB	53	48	96	138
17	KUMAR	57	M	AB	52	41	95	145
18	SEKAR	50	M	AB	46	38	92	149
19	DAVID	54	M	N	44	39	45	144
20	VELU	40	M	AB	39	31	49	146
21	MUMTAJ	49	F	AB	38	29	289	138
22	MURUGAN	43	M	AB	59	54	243	138
23	GURUNATHAN	50	M	AB	25	17	275	136
24	RAMKUMAR	21	M	AB	43	41	178	141
25	BALU	35	M	AB	63	54	328	142
26	PAVITHRA	28	F	N	68	52	36	146
27	SANKAR	52	M	AB	42	35	89	148
28	SUGUNA	45	F	AB	53	42	156	139
29	GOTHANDAM	58	M	AB	63	59	326	136
30	LAKSHMIPATHY	41	F	AB	65	61	537	147
31	AARTHI	16	F	AB	46	39	132	45
32	KARTHIKEYAN	27	M	AB	22	15	138	148
33	RAJA	46	M	AB	39	30	93	138
34	KANNAMAL	32	F	AB	58	54	78	139

SL.NO	SEIZURE GROUP							
	NAME	AGE	SEX	EEG N/AB	S.PROLACTIN (mcg/L)		RBS	S.Na+
					30 min	2hr		
35	JAYA	38	F	AB	62	60	106	136
36	SELVI	56	F	AB	66	63	109	143
37	GOPAL	39	M	AB	45	41	132	148
38	IRUDHYARAJ	26	M	AB	38	35	187	136
39	MOHAN	46	M	AB	48	46	109	134
40	ESWARI	47	F	N	55	52	104	132
41	KAVITHA	20	F	AB	61	50	266	126
42	NARAYANAN	27	M	AB	44	34	78	144
43	JANAKI	55	F	AB	43	39	92	147
44	NABISHA	57	F	AB	20	19	147	139
45	RAHAMATH BEE	47	F	AB	61	57	636	135
46	PADMANABU	41	M	AB	57	45	142	143
47	PERUMAL	21	F	AB	54	39	98	141
48	KRISHNAN	53	M	AB	39	32	87	148
49	GOMATHI	18	F	AB	43	40	81	147
50	KEERTHI	46	F	AB	52	46	79	142
51	HARIKRISHNAN	40	M	AB	59	48	195	137
52	VIKARAM	20	M	AB	49	46	146	138
53	MADAN	27	M	N	45	42	125	136
54	RAVI	36	M	AB	22	18	120	148
55	BABU	28	M	AB	28	19	118	141
56	KOTTAMMAL	51	F	AB	45	36	104	36
57	MURUGAN	42	M	AB	25	28	498	135
58	PRASANTH	39	M	AB	18	22	107	147
59	SARAN	28	M	AB	29	27	78	143
60	VINOTH	32	M	AB	37	39	94	148
61	VETRIVEL	27	M	AB	48	36	106	142

SL.NO	SEIZURE GROUP							
	NAME	AGE	SEX	EEG N/AB	S.PROLACTIN (mcg/L)		RBS	$S.Na^+$
					30 min	2hr		
1	ESWARI	55	F	AB	51	45	245	132
2	SUSSELA	36	F	AB	46	39	123	136
3	FAZAL	32	M	AB	41	36	109	139
4	ZEENATH BEE	52	F	AB	57	49	88	126
5	VELAYUDAM	65	M	AB	40	32	308	143
6	RENUGA	42	F	AB	53	45	563	124
7	MANNAR	59	M	AB	49	44	254	32
8	PUNITHA	32	F	AB	59	52	123	136
9	PICHAYAMMAL	35	F	AB	62	51	123	39
10	SARALA DEVI	50	F	AB	66	56	112	138
11	PAREMESHWARI	62	M	N	56	49	115	139
12	SHANKAR	35	M	AB	52	42	152	141
13	GEETHA	42	F	AB	47	39	43	128
14	RAJENDRAN	52	M	AB	42	35	128	146
15	SUNDARAM	35	M	AB	61	52	127	135
16	VATCHALA	40	F	AB	53	48	96	138
17	KUMAR	57	M	AB	52	41	95	145
18	SEKAR	50	M	AB	46	38	92	149
19	DAVID	54	M	N	44	39	45	144
20	VELU	40	M	AB	39	31	49	146
21	MUMTAJ	49	F	AB	38	29	289	138
22	MURUGAN	43	M	AB	59	54	243	138
23	GURUNATHAN	50	M	AB	25	17	275	136
24	RAMKUMAR	21	M	AB	43	41	178	141
25	BALU	35	M	AB	63	54	328	142
26	PAVITHRA	28	F	N	68	52	36	146
27	SANKAR	52	M	AB	42	35	89	148
28	SUGUNA	45	F	AB	53	42	156	139
29	GOTHANDAM	58	M	AB	63	59	326	136
30	LAKSHMIPATHY	41	F	AB	65	61	537	147
31	AARTHI	16	F	AB	46	39	132	45
32	KARTHIKEYAN	27	M	AB	22	15	138	148
33	RAJA	46	M	AB	39	30	93	138
34	KANNAMAL	32	F	AB	58	54	78	139
35	JAYA	38	F	AB	62	60	106	136
36	SELVI	56	F	AB	66	63	109	143
37	GOPAL	39	M	AB	45	41	132	148
38	IRUDHYARAJ	26	M	AB	38	35	187	136

SL.NO	SEIZURE GROUP							
	NAME	AGE	SEX	EEG N/AB	S.PROLACTIN (mcg/L)		RBS	$S.Na^{+}$
					30 min	2hr		
39	MOHAN	46	M	AB	48	46	109	134
40	ESWARI	47	F	N	55	52	104	132
41	KAVITHA	20	F	AB	61	50	266	126
42	NARAYANAN	27	M	AB	44	34	78	144
43	JANAKI	55	F	AB	43	39	92	147
44	NABISHA	57	F	AB	20	19	147	139
45	RAHAMATH BEE	47	F	AB	61	57	636	135
46	PADMANABU	41	M	AB	57	45	142	143
47	PERUMAL	21	F	AB	54	39	98	141
48	KRISHNAN	53	M	AB	39	32	87	148
49	GOMATHI	18	F	AB	43	40	81	147
50	KEERTHI	46	F	AB	52	46	79	142
51	HARIKRISHNAN	40	M	AB	59	48	195	137
52	VIKARAM	20	M	AB	49	46	146	138
53	MADAN	27	M	N	45	42	125	136
54	RAVI	36	M	AB	22	18	120	148
55	BABU	28	M	AB	28	19	118	141
56	KOTTAMMAL	51	F	AB	45	36	104	36
57	MURUGAN	42	M	AB	25	28	498	135
58	PRASANTH	39	M	AB	18	22	107	147
59	SARAN	28	M	AB	29	27	78	143
60	VINOTH	32	M	AB	37	39	94	148
61	VETRIVEL	27	M	AB	48	36	106	142

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